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Effects of vasopressors on circulation in the porcine abdominal island flap model

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Summary *Background:* During reconstructive surgical procedures, systemic vasopressors are frequently used to maintain normal blood pressure. However, questions have arisen regarding the pharmacologic effects of vasopressors on flap circulation. Many plastic surgeons have expressed concern about the possibility of impaired flap circulation caused by the vasoconstrictive effect of the drugs. However, the opposing argument exists that the increase in mean arterial pressure from vasoactive agents may improve flap perfusion. The purpose of this study was to evaluate the effect of commonly used vasopressors on flap circulation.
Methods: The vertical rectus abdominis myocutaneous (VRAM) island flap was raised in five female pigs (38.2∼40.7 kg). Hemodynamic parameters were measured continuously by a carotid arterial catheter. A bi-directional transonic vascular doppler flow probe and Laser Doppler perfusion monitor (LDPM) unit were applied to record the continuous change in pedicle artery flow and microvascular perfusion following intravenous administration of dopamine (3, 5, 10μg/kg/minute), dobutamine (1.25, 2.5, 5μg/kg/minute), and norepinephrine (0.05, 0.1, 0.2μg/kg/minute).
Results: Both microvascular perfusion and pedicle flow were generally proportional to the mean arterial pressure, and all three vasopressors improved flap perfusion and pedicle flow without deleterious effects. Norepinephrine showed the highest microvascular perfusion and dobutamine showed the highest pedicle flow rate. The mean blood pressure was the only statistically significant factor to affect both microvascular perfusion and pedicle flow ($p < 0.0001$).

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Conclusion: Our results strongly suggest that the foremost three vasopressors can be used for flap surgery without deterioration, and that the maintenance of adequate systemic blood pressure is crucial for good flap circulation.

Introduction

Vasopressors are useful tools for the treatment of hypotension under general anesthesia. However, questions exist regarding the pharmacologic effect of systemic vasopressor on flap surgery. Many plastic surgeons are concerned about the theoretical risk of vasospasm or venous congestion caused by the peripheral vasoconstrictive effect of the drugs, which may lead to flap complications. Furthermore, flap ischemia or thrombosis can occur as a result of decreased flap perfusion. Although some studies have demonstrated detrimental effects of vasoconstrictors,[1,2] contradictory data have been published that show that the vasoactive agents may improve flap perfusion with an increase of mean arterial pressure (MAP).[3,4] There is no consensus regarding the use of vasopressor agents in flap surgery.[5,6]

It is important for plastic surgeons and anesthesiologists to understand the effects of vasopressors on flap circulation. In their absence, most clinicians usually try to treat intraoperative hypotension with intravenous administration of crystalloid and colloid fluid.[7] However, this may cause edema and hemodynamic imbalance without a further increase in cardiac output. At present, only a few studies report which vasopressor can be used safely for both flap circulation and patient status.

Sympathomimetic vasopressor agents like dopamine, dobutamine and norepinephrine are commonly used to correct a hypotensive crisis by increasing systemic mean arterial pressure. Mechanism of these vasoactive agents differ from each other depending on their adrenergic effect. First, dopamine is a precursor of epinephrine and norepinephrine, which acts on both α and β receptors as well as dopaminergic receptors for the correction of hemodynamic imbalances. Dobutamine, predominantly a β_1-receptor agonist, increases cardiac contractility with minimal effect on blood pressure. Finally, norepinephrine acts on both α and β_1 adrenergic receptors, but has a more α-receptor dominant tendency. Its vasoconstrictive effect is a concern, however, because it leads to a more significant effect on blood pressure than on heart rate. These three drugs are useful options for the treatment of hypotension when selected appropriately for each situation.

The purpose of this study was to evaluate the effect of commonly used vasopressors on flap circulation. We evaluated the changes in pedicle artery blood flow of a porcine abdominal island flap model with systemic administration of three agents - dopamine, dobutamine and norepinephrine.

Material and methods

Animal anesthetic and instrumentation

Five healthy female pigs weighing from 38.2 to 40.7 kg (mean weight, 39.5 kg) were used in this study. All experiments were approved by the Institutional Animal Use and Care Committee of Korea University College of Medicine under protocol number 2018–0010. After administration of a single intramuscular injection of alfaxalone (4 mg/kg), xylazine (2 mg/kg), azaperone (6 mg/kg) and atropine (0.5 mg/kg), intravenous alfaxalone (1∼2 mg/kg), xylazine (0.5 mg/kg) and isoflurane-maintained anesthesia (1.5∼2.0% atm) facilitated mechanical ventilation and surgical dissection. Carotid artery catheter, jugular venous catheter, and peripheral ear venous catheters were placed for drug delivery and hemodynamic status monitoring.

Surgical procedure

In each pig, a unilateral vertical rectus abdominis myocutaneous (VRAM) island flap was elevated by 18 × 9 cm rectangular skin island just lateral to the midline (Figure 1, left). The deep inferior epigastric vascular arteries and veins were transected, and surgical dissection proceeded from caudal to cephalic direction. Superior epigastric pedicles were

Figure 1 **(Left)** VRAM island flap based superior epigastric pedicle was elevated **(Right)** The vascular laser doppler probe (DVM-4500; Hadeco, Inc. Kanagawa, Japan) was placed and the pedicle was put into the groove of the probe.

Figure 2 **(Left)** Laser doppler perfusion monitor unit (LPDM, Perimed AB, Jarfalla, Sweden) showed measurement of microvascular perfusion. **(Right)** The integrating doppler flow probe was attached to the midpoint of skin flap.

Table 1 Drug infusion rates.

	Concentration (μg/mL)	First infusion rate (μg/kg/min)	Second infusion rate (μg/kg/min)	Third infusion rate (μg/kg/min)
Dopamine	100	3.0	5.0	10.0
Dobutamine	100	1.25	2.5	5.0
Norepinephrine	4	0.05	0.1	0.2

isolated, and the proximal side of the flap was separated using Ligasure electrocautery (Medtronic, Minneapolis, MN, USA). Additional pedicle dissection was performed to provide space to place the Laser Doppler probe. All procedures were performed under a constant operating table temperature maintained with a temperature controller.

Outcome measurements

Pedicle blood flow

To measure blood flow through the superior epigastric artery, a bi-directional transonic vascular doppler flow probe (DVM-4500; Hadeco, Inc. Kanagawa, Japan, Figure 1, right) was placed, and the pedicle was put into the groove of the probe. To minimize noise caused by arterial movement, fibrin sealant (Tisseel; Baxter, Deerfield, IL, USA) was applied.

Microvascular perfusion

A Laser Doppler perfusion monitor (LDPM) unit (Perimed AB, Jarfalla, Sweden) was applied to measure the microvascular perfusion. A doppler flow probe (Perimed Probe 407, Figure 2) was attached at the skin flap midpoint.

Vasopressor infusion

Three doses of each of three drugs (dopamine, dobutamine, norepinephrine) were administered under the dose control of an infusion pump (Table 1). The dosage of each drug was determined from a pilot study using the recommended dose for a person weighing 40.0 kg. After a one-hour stabilization period elapsed, baseline hemodynamic parameters and flow were recorded. Dopamine was infused at a 3.0μg/kg/minute until stable hemodynamic was reached, and data were recorded. Dopamine was continuously infused at rates of 5.0μg/kg/minute and 10.0μg/kg/minute and outcomes were recorded for each dose. A 30-minute period elapsed before infusion of the next drug to allow physiological variables to return to baseline. In a similar way, dobutamine (1.25, 2.5, 5.0μg/kg/minute) and then norepinephrine (0.05, 0.1, 0.2μg/kg/minute) were infused and the responses were recorded. At the end of the experiment, each pig was euthanized by cardiac arrest from injection of potassium chloride (2 mmol/kg). The infusion order of three drugs was randomized for each pig to prevent differences in the effect of the injection sequence.

Statistical analysis

All statistical analyses were performed using SAS version 9.4 software (SAS Institute Inc., Cary, NC, USA) in consultation with an independent medical statistician who did not participate in the study. A linear mixed models (LMM) was fitted to the data, considering factors such as drug, mean arterial pressure (MAP), and dosage. Tukey-Kramer post-hoc analysis was used for multiple comparisons. Simple linear regression was used to account for the effect of mean arterial pressure on microvascular perfusion and pedicle flow rate for each drug. For all analyses, a value of $p < 0.05$ was considered statistically significant.

Results

Systemic physiologic parameters and mean values for microvascular perfusion units and pedicle flow at baseline and for each dosage are shown in Table 2.

Mean arterial pressure

Dopamine, dobutamine, and norepinephrine increased systemic mean arterial pressures in a dose- dependent manner.

Table 2 Hemodynamic parameter after infusion of dopamine, dobutamine and norepinephrine at three doses.

Drug dose	HR, beats/min	SBP / DBP, mmHg	MAP, mmHg	Microvascular Perfusion units	Mean pedicle flow, ml/min
Dopamine					
baseline	68 ± 8	57 ± 9 / 36 ± 3	49 ± 8	98.6 ± 69.2	21.0 ± 14.4
3 μg/kg/min	68 ± 8	62 ± 9 / 40 ± 7	48 ± 5	102.2 ± 73.7	21.6 ± 15.0
5 μg/kg/min	75 ± 12	65 ± 10 / 42 ± 8	49 ± 8	104.5 ± 75.3	21.6 ± 14.2
10 μg/kg/min	85 ± 11	70 ± 9 / 43 ± 8	54 ± 8	108.2 ± 75.5	22.7 ± 12.8
Dobutamine					
baseline	68 ± 8	63 ± 11 / 39 ± 11	50 ± 10	117.6 ± 81.1	20.0 ± 10.4
1.25 μg/kg/min	92 ± 15	85 ± 7 / 46 ± 8	62 ± 9	126.0 ± 76.0	27.0 ± 8.9
2.5 μg/kg/min	106 ± 35	84 ± 10 / 42 ± 8	58 ± 8	127.0 ± 76.0	24.8 ± 10.7
5.0 μg/kg/min	137 ± 32	83 ± 11 / 48 ± 15	59 ± 10	123.1 ± 71.1	21.8 ± 12.1
Norepinephrine					
baseline	67 ± 13	53 ± 15 / 36 ± 10	42 ± 10	90.8 ± 68.2	21.7 ± 15.5
0.05 μg/kg/min	77 ± 13	72 ± 15 / 47 ± 11	54 ± 8	145.7 ± 104.4	22.3 ± 14.0
0.1 μg/kg/min	85 ± 20	86 ± 13 / 51 ± 11	67 ± 10	114.9 ± 71.3	22.6 ± 12.5
0.2 μg/kg/min	106 ± 26	94 ± 9 / 54 ± 9	63 ± 18	127.2 ± 84.0	23.0 ± 12.1

※ HR, heart rate; SBP, systemic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure.
※ Each parameter shows the mean ± SD from five pigs. In our dose protocol, dopamine was infused at a 3, 5, and 10 μg/kg/minute. Dobutamine (1.25, 2.5, and 5 μg/kg/minute) and norepinephrine (0.05, 0.1, and 0.2 μg/kg/minute) were also infused at each dose.

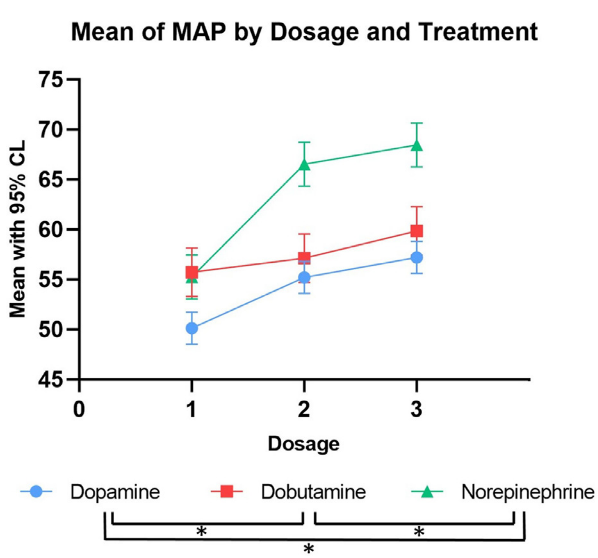

Figure 3 Mean of MAP (mmHg) by dosage and the type of drug. (*$p < 0.05$).

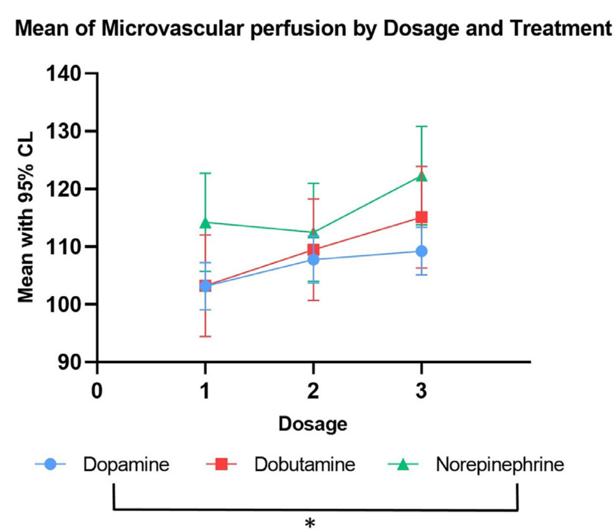

Figure 4 Mean of microvascular perfusion by dosage and the type of drug (*$p < 0.05$).

When the linear mixed modeling for mean arterial pressures was conducted after adjusting for other covariates, both the type and dose of the drug significantly affected the mean arterial pressure ($p < 0.05$). In further Tukey-Kramer post-hoc analysis, the mean arterial pressure increased in the order of norepinephrine, dobutamine, and then dopamine (Figure 3).

Table 3 The results of type III tests of fixed effects for microvascular perfusion (PU).

Factor	with MAP variate		without MAP variate	
	F value	*p* value	*F* value	*p* value
Drug	0.35	0.7136	4.95	0.0399
Dosage (Drug)	2.07	0.0953	1.3	0.2961
MAP	27.07	<0.0001	N/A	N/A

Microvascular perfusion

Dopamine, dobutamine and norepinephrine increased microvascular perfusion unit in a dose-dependent manner. (Figure 4) When three variates were analyzed, - including the type of drug, dosage, and mean arterial pressure, a significant difference was seen only for MAP (Table 3, $p < 0.05$). Without applying a mean arterial pressure variate, however, a significant difference was seen for the type of drug ($p < 0.05$). When Tukey-Kramer post-hoc

Table 4 Post-hoc analysis of the LMM model for microvascular perfusion (PU) without MAP variate.

Effect	Compare group		Mean difference	*t* value	Prob>[t]	Adj *p*
Drug	Dopamine	Norepinephrine	−10.47	−3.14	0.0138	0.033
	Dopamine	Dobutamine	−2.72	−0.82	0.4374	0.7032
	Norepinephrine	Dobutamine	7.74	2.32	0.0486	0.1093

※ Adj *p* indicates adjusted *p*-value obtained by Tukey-Kramer post-hoc test to identify differences between the experimental groups.

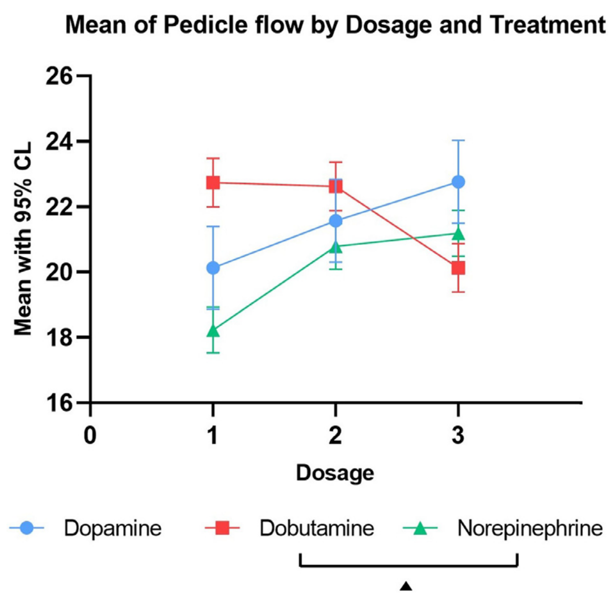

Figure 5 Mean of pedicle flow rate (ml/min) by dosage and the type of drug (▲ means borderline significance, $p = 0.073$).

Table 5 Type III tests of fixed effects for pedicle flow (PF).

Factor	With MAP variate		Without MAP variate	
	F value	*p* value	*F* value	*p* value
Drug	15.85	0.0017	3.32	0.0892
Dosage (Drug)	2.23	0.0748	3.16	0.0199
MAP	33.34	<0.0001	N/A	N/A

analysis was performed (Table 4), norepinephrine showed better efficacy to increase microvascular circulation than dopamine ($p < 0.05$).

Pedicle blood flow

Dopamine and norepinephrine showed a dose-dependent increase in pedicle blood flow. (Figure 5) Dobutamine also increased the pedicle blood flow at the initial dose; however this effect disappeared and pedicle blood flow slightly decreased at the second and third infusion doses. When analysis was performed using three variates, including the type of drug, dosage, and mean arterial pressure, both MAP and the type of drug showed significant differences (Table 5, $p < 0.05$). In post-hoc analysis, dobutamine showed a borderline significant increase in pedicle blood flow compared to norepinephrine (Table 6, $p = 0.073$).

Linear regression analysis

A linear regression analysis of mean arterial pressure on percent (%) change in microvascular perfusion unit and pedicle flow rate was done for each drug group. We hypothesized that increasing the mean arterial pressure with systemic administration of a vasopressor would increase microvascular perfusion and pedicle flow rates, and that the increases would vary with the drug administered.

First, dopamine showed a proportional relationship with MAP in both pedicle flow and cutaneous perfusion. (Figure 6, $p < 0.05$) Dubutamine also showed a proportional relationship with MAP and microvascular perfusion ($p < 0.05$); however, there was no positive correlation between MAP and pedicle flow. (Figure 7) Finally, norepinephrine showed a significant proportional relationship between MAP and pedicle flow (Figure 8, $p < 0.05$). It also showed a positive correlation between MAP and microvascular perfusion, but without statistical significance ($p > 0.05$).

Discussion

Results of this study showed that microvascular perfusion and mean pedicle flow tend to depend on mean arterial pressure. Mean arterial pressure was the only factor significantly affecting both microvascular perfusion and the pedicle flow rate (Table 3 and 5, $p < 0.05$) All three vasopressors improved flap perfusion by means of increased mean arterial pressure, and there were no deleterious outcomes in cutaneous perfusion and pedicle flow.

Norepinephrine showed the highest mean value of mean arterial pressure and microvascular perfusion. It is known that less than 0.03 μg/kg/minute of norepinephrine may uncover the effects of β_1 - adrenergic stimulation, and the usual infusion rates of greater than 0.05μg/kg/minute elicit peripheral vasoconstriction from α-adrenergic stimulation.[8] In our study, norepinephrine was infused at rates of 0.05, 0.1, 0.2μg/kg/minute, thus we could see both α and β_1 adrenergic effect of norepinephrine. The α-adrenergic activity has been shown to impede flap flow and be harmful to the peripheral circulation, occasionally resulting in loss of digits or extremities.[9] Many flap surgeons and anesthesiologists avoid norepinephrine because of the vasoconstrictive effect of α-adrenergic activity; however, it seems that the β_1 activity effect to increase blood pressure overcame its peripheral effects in our study.

Dobutamine showed the highest mean pedicle flow rate because of its β-adrenergic effect associated with cardiac output. Tuttle et al. reported that its activity on the α receptors controlling arterial resistance was weak relative to its activity on the β receptors controlling myocardial

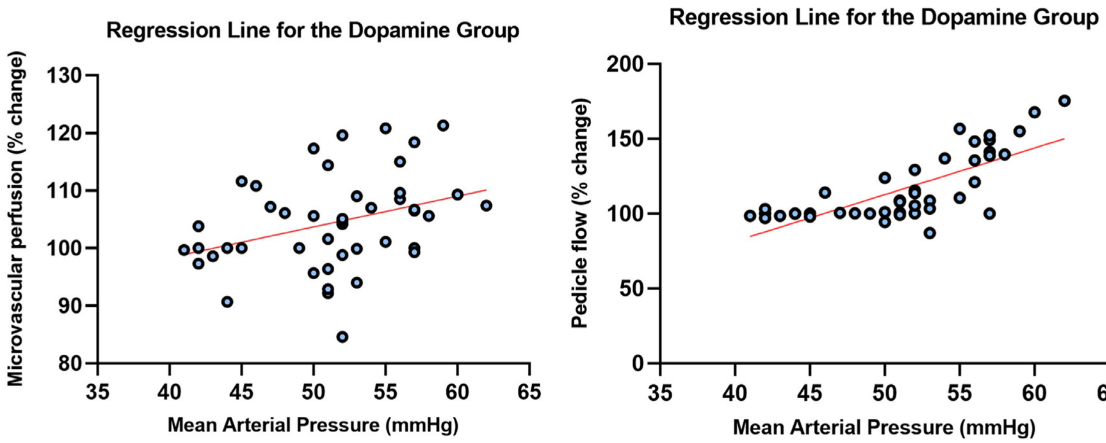

Figure 6 Linear regression between mean arterial pressure and microvascular perfusion / mean pedicle flow rate (% change) in dopamine group **(Left)** Relationship with MAP in cutaneous perfusion, slope is 0.533 ($p = 0.020$) **(Right)** Relationship with MAP in pedicle flow rate, slope is 3.114 ($p = 0.000$).

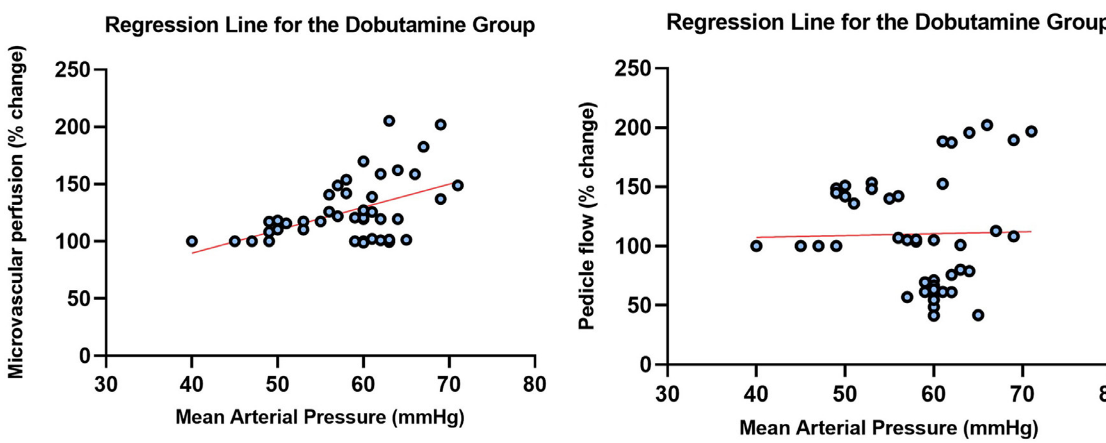

Figure 7 Linear regression between mean arterial pressure and microvascular perfusion / mean pedicle flow rate (% change) in dobutamine group **(Left)** Relationship with MAP in cutaneous perfusion, slope is 2.003 ($p = 0.001$) **(Right)** Relationship with MAP in pedicle flow rate, slope is 0.152 ($p = 0.887$).

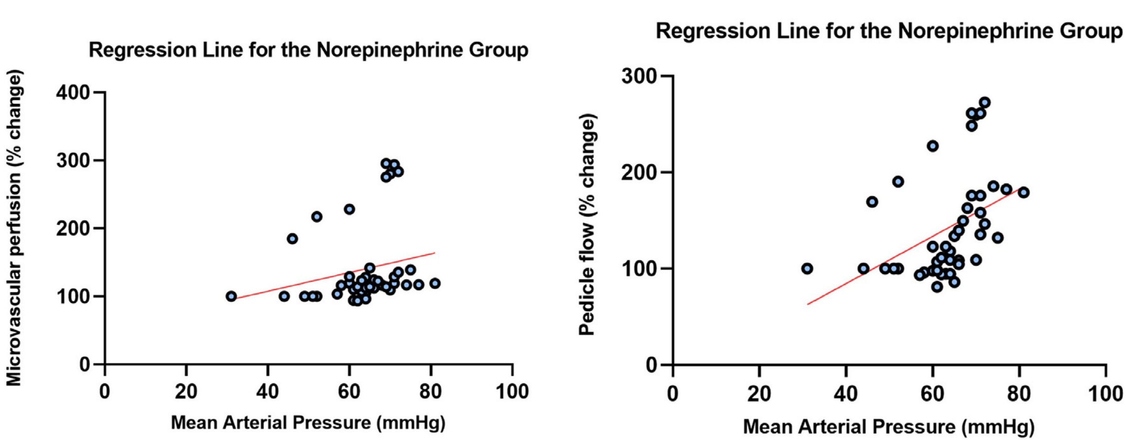

Figure 8 Linear regression between mean arterial pressure and microvascular perfusion / mean pedicle flow rate (% change) in norepinephrine group **(Left)** Relationship with MAP in cutaneous perfusion, slope is 1.375 ($p = 0.149$) **(Right)** Relationship with MAP in pedicle flow rate, slope is 2.450 ($p = 0.004$).

Table 6 Post-hoc analysis of the LMM model for pedicle flow (PF) without MAP variate.

Factor	Compare group		Estimate	*t* value	Prob>[t]	Adj *p*
Drug	Dopamine	Norepinephrine	1.153	1.78	0.1131	0.236
	Dopamine	Dobutamine	−0.533	−0.82	0.4346	0.700
	Norepinephrine	Dobutamine	−1.687	−0.2.6	0.0315	0.073

※Adj *p* indicates adjusted *p*-value obtained by Tukey-Kramer post-hoc test to identify differences between the experimental groups.

contractility.[10] Scholz et al. reported that dobutamine infusions of 4 and 6μg/kg/minutes increased mean and maximum blood flows and the increases were accompanied by increased cardiac output.[11] In our study, dobutamine was infused at rates of 1.25, 2.5 and 5μg/kg/min and produced results consistent with Scholz.

Dobutamine, however, frequently causes tachycardia; so, its use requires strict heart rate monitoring. In a number of cases, premature termination of dobutamine infusion was necessary because of tachycardia caused by the drug's inodilatory effects.[12] In our study, it also produced similar results, and it needed more stabilization time to return to baseline after cessation. Roubille et al. reported that dobutamine-induced tachycardia could lead to loss of the beneficial cardiac effect of the drug by hampering filling.[13] As dobutamine dose increased, severe tachycardia led to cardiac filling impairment and reflexive systemic vasoconstriction, and the net effect of dobutamine was reduced pedicle flow while maintaining blood pressure. Thus, it should be used with caution.

Dopamine is a sympathomimetic amine vasopressor for correction of hemodynamic imbalances. Its effect varies depending on dosage. A dose of 3-10 μg/kg/minute caused β-adrenergic stimulation, and infusion rates of more than 10 μg/kg/minute caused peripheral vasoconstriction due to α-adrenergic stimulation.[8] We infused at rates of 3, 5, 10μg/kg/minute; thus, we could see the β-adrenergic effect of dopamine relatively. High doses of commonly used β-agonists such as dopamine have been shown to improve cardiac output and systemic blood pressure.[14] In our study, dopamine showed a relatively weaker effect on mean arterial pressure and microvascular perfusion than norepinephrine and dobutamine. Linear regression of mean arterial pressure on percent change in pedicle flow, however, showed the highest slope estimate with statistical significance. (Figure 6, $p < 0.05$)

As mentioned previously, mean arterial pressure is the most significant factor in mean microvascular perfusion and mean pedicle flow. (Table 3 and 5, $p < 0.05$) From this aspect, we hypothesized that the percent change of microvascular perfusion and pedicle flow rates following an increase in mean arterial pressure would vary from drug to drug. In a simple linear regression analysis of microvascular perfusion, slope of the regression line decreased in the order of dobutamine, norepinephrine, then dopamine. This means that dobutamine was the most effective drug in increasing microvascular perfusion in response to a change in mean arterial pressure. Hence, to improve perfusion without a significant rise of blood pressure, dobutamine would be the drug of choice. In a simple linear regression analysis of pedicle flow, slope of the regression line decreased in the order of dopamine, norepinephrine then dobutamine. This demonstrated that dopamine was the most effective to increase pedicle flow rate in response to change of MAP. The low efficacy of dobutamine at higher doses may be caused by impaired filling due to tachycardia and reflexive vasoconstriction. Because increasing the infusion dose of dobutamine led an increase of blood pressure while reducing pedicle flow, it did not result in a positive slope. All three drugs except dobutamine in pedicle flow showed positive slope estimates in two linear regression analyses; thus, it can be concluded that these vasopressors at commonly used doses do not adversely affect flap circulation.

An important premise of this study is that superior epigastric pedicle was isolated without any adventitial stripping. It means that whole procedure of this study was carried out without sympathetic denervation of the flap, which may injury to vascular smooth muscle and endothelium. The total sympathectomy result in a microvascular perfusion and pedicle flow that have different vascular tones and different reaction to the systemic and local vasoactive stimuli.[2] In our result, however, the flap with the intact sympathetic tone appears to response to α-adrenergic activity of vasopressors, similar to the intact myocutaneous unit. It is planned that the effects by sympathetic denervation of the flap pedicle would be analyzed in our follow-up studies.

There have been several experimental studies using a porcine model to demonstrate the relationship between vasopressor agents and flap perfusion. Massey et al. [2] compared the effect of systemic phenylephrine and epinephrine on pedicle artery and microvascular perfusion in a porcine model of myocutaneous rotational flap. In this study, however, we have shown the effects of three other vasopressors (dopamine, dobutamine and norepinephrine) in an abdominal island flap model. Also, the variable factors in our study were strictly controlled by a linear mixed model for three group comparison. Cordeiro et al. [15] showed that flap blood flow increased with dobutamine administration and remained unchanged with dopamine administration. They used a vascular doppler flow probe for continuous monitoring of arterial flow, while we used both a vascular doppler flow probe and a Laser Doppler perfusion monitor with a skin probe to detect changes in microvascular perfusion.

In our study, we used the linear mixed model(LMM) because of its usefulness in analyzing repeated-measure data.[16] LMM can analyze both time-dependent covariates and a number of fixed effects. All factors such as type of drug, dosage nested in drug and the interaction effect between time and dosage can be incorporated into this statistical model. Furthermore, the effects of each factor may be corrected by one another to explain the change of dependent variables according to individual independent variables in a single regression formula. Therefore, LMM model is an appropriate method to assess the effect of multiple factors like our experimental study.

Our study had several limitations. First, microvascular perfusion unit and pedicle flow rates were measured after an island flap was elevated and its hemodynamic parameters reached a baseline for timing comparisons. Therefore, the results of this study were limited to the phase of post flap elevation in the intraoperative period and may not be transferable to the whole intraoperative period or indeed the postoperative period. Second, our experimental design based on VRAM island flap may limit the generalizability of the conclusion. The flap in this study is relatively close to the heart and could not reflect the factor like distal resistance in the lower extremity. In many clinical situations, the critical region of question is in the lower extremity. Initially, we also planned an island flap in the lower extremity based femoral pedicle. During the preliminary experiment, however, the plan was changed to VRAM island flap based superior epigastric pedicle because of the appropriate pedicle size with a reliable anatomic consistence. If further study including lower extremities is followed, it would be more evident. The final limitation was the relatively small sample size. Originally, we intended to decide which drug was better able to perfuse a hypotensive flap, but some results of post-hoc analyses were not significant. If studies are done with greater sample sizes, more meaningful results may be generated.

In this study, we confirmed that both microvascular perfusion and pedicle flow were generally proportional to mean arterial pressure, and all three vasopressors improved flap perfusion and pedicle flow without deleterious effects. The regression line slope estimate of dobutamine on microvascular perfusion was higher than other drug, demonstrating that dobutamine was the most effective drug to increase cutaneous perfusion in response to change of mean arterial pressure Furthermore, dobutamine, by its inotropic action, produced the highest mean pedicle flow at a low dose. However, dobutamine should be used with caution because of the potential for severe tachycardia and paradoxical decrease of pedicle flow. Norepinephrine showed the highest mean value of blood pressure and microvascular perfusion among the three drugs. It appears that β_1 activity with increasing blood pressure overcame its peripheral effect in our study. Dopamine showed a relatively weaker effect on mean arterial pressure and microvascular perfusion than norepinephrine and dobutamine. In the linear regression of mean arterial pressure on percent change in pedicle flow rate, however, it shows the highest slope estimate with statistical significance.

Conclusion

In conclusion, our results strongly suggest that the foremost three vasopressors can be used for flap surgery without deterioration, and that the maintenance of adequate systemic blood pressure is crucial for good flap circulation.

Declaration of Competing Interest

We have no potential conflicts of interest relevant to this article to report.

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