의학박사 학위논문

심장수술 후 발생한 쇼크의 치료로서 Dopamine 과 Norepinephrine 에 대한 비교 연구

Dopamine versus Norepinephrine
in the Management of Shock after Cardiac Surgery

울산대학교대학원

의 학 과

임 주 영

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지도교수 정 성 호

이 논문을 의학박사 학위 논문으로 제출함

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울산대학교 대학원

의 학 과

임 주 영

임주영의 의학박사학위 논문을 인준함

심사위원 정성호 (인)

심사위원 김준범 인

심사위원 주석중 인

심사위원 정철현 인

심사위원 정재승 인

울 산 대 학 교 대 학 원

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Background: Shock after cardiac surgery is a frequent but life-threatening condition. Intensive management with the use of inotropic agents is essential to treat post-cardiotomy shock. However, the ideal vasoactive agent remains controversial. We compared dopamine and norepinephrine to treat post-cardiac surgery shock.

Methods: Patients with shock following cardiac surgeries were randomly assigned to receive either dopamine or norepinephrine as first-line vasopressors. Persistent shock despite maximal doses of drug infusion (dopamine 20 mcg/kg/min, norepinephrine 0.2 mcg/kg/min) or intolerance to first-line therapy owing to the development of tachyarrhythmia, necessitated the administration of second-line vasoactive inotropes (epinephrine and vasopressin). The primary endpoint was new-onset tachyarrhythmia (supraventricular, ventricular, or sinus tachycardia) during drug infusion. Secondary endpoints included all-cause mortality, requirement of second-line vasoactive inotropes, and major postoperative complications observed within 30 days of drug initiation.

Results: At the planned interim analysis of 100 patients (48 administered dopamine and 50 norepinephrine, 2 drop-outs), a futility boundary for the primary endpoint was crossed, and the study was discontinued. Intergroup baseline characteristics were similar. New-onset tachyarrhythmia occurred in 12 patients in the dopamine and 1 patient in the norepinephrine group, showing a statistically significant difference (odds ratio [OR] 16.3, 95% confidence interval [CI], 2.0–131.3, P=0.009). The requirement for additional vasoactive inotropes was significantly more common in the dopamine group (OR 52.7, 95% CI 13.7–202.7, P<0.001). Other components of secondary endpoints showed intergroup similarity.

Conclusions: Dopamine used as a first-line vasopressor for shock after cardiac surgery was associated with a higher risk of tachyarrhythmic events and a greater need for second-line vasoactive inotropes than that observed with norepinephrine.

차 례

표 및 그림 목차

Introduction

Various types of shock may occur in the postoperative period after cardiovascular surgery.[1)] Usually, shock occurs secondary to hypovolemia, low cardiac output after ischemia-reperfusion injury, vasodilation caused by an inflammatory response during cardiopulmonary bypass,[2,3)] or a combination of these etiologies. Postoperative shock is a life-threatening condition; thus, immediate fluid resuscitation and the administration of appropriate vasoactive inotropic drugs are essential for its management. The most commonly used and recommended vasoactive drugs that serve as first-line therapy in patients with shock are dopamine and norepinephrine.[4,5)] These drugs act on both, the alpha- and beta-adrenergic receptors, albeit to a different degree, Thus, the effect of these drugs on cardiac output, other organ perfusion, peripheral circulation, and cardiac contractility differs.[6,7)] However, there is a lack of reliable evidence regarding the comparative efficacy of each agent, particularly in the setting of post-cardiac surgery shock. Recently, a prospective randomized trial performed by De Backer et al.[8)] reported a subgroup analysis in patients with cardiogenic shock. The authors observed that dopamine was associated with a higher early mortality rate and arrhythmia than that observed with norepinephrine. They suggested that the contributory effect of a higher heart rate or arrhythmia observed with dopamine leads to the occurrence of ischemic events and a higher early mortality with caution. Patients undergoing cardiac surgery are highly vulnerable to develop postoperative arrhythmia because of several perioperative factors.[9)] Therefore, the administration of vasoactive agents that might precipitate arrhythmia could be unsafe in the treatment of shock in this patient population. This study was designed to compare the efficacy of dopamine and norepinephrine in the treatment of shock in patients undergoing cardiovascular surgery. We hypothesized that dopamine would demonstrate a higher arrhythmogenic effect than that produced by norepinephrine.

Methods

Patient selection

We performed a prospective, single-blind randomized trial at Asan Medical Center, Seoul, Korea between June 15, 2017 and January 15, 2018. Our study included patients who were admitted to the cardiac surgery intensive care unit (CSICU) after cardiovascular surgery.

This study was approved by the Institutional Review Board (IRB) of our hospital (IRB number: 2017-0699). Written informed consent was obtained from all patients before the operation with the understanding that anesthetized patients would be unable to sign informed consent documents after enrollment and following the development of shock.

Adults (age 19–79 years) who developed shock in the ICU after cardiovascular surgery were eligible for enrollment. Shock was defined as mean blood pressure <70 mmHg or systolic blood pressure <100 mmHg despite adequate fluid resuscitation. Initial fluid resuscitation included the administration of a minimum of 1 L of crystalloid and 500 mL of colloid or blood products. However, based on the underlying cardiac and renal function of patients, initial fluid administration could be restricted. Signs of tissue hypoperfusion such as lactate levels >2 mmol/L and the presence of oliguria were defined as shock. If a patient was admitted to the ICU and was receiving a dopamine or norepinephrine infusion that had been initiated in the operating room, these agents were tapered, and the patient was observed. If the patient redeveloped shock in the ICU, the patient was eligible for enrollment. Patients excluded from the study were: those who had already received rescue drug infusions such as epinephrine or vasopressin or mechanical circulatory support in the operating room, those with chronic rhythm disorders such as chronic supraventricular arrhythmia, those with permanent pacemaker or implantable cardiac defibrillator insertion before surgery, and those who underwent emergency operations or heart transplantation.

Study protocol

Using a computer-generated randomization list of variable permuted blocks of 2, 4, and 6, a patient demonstrating shock in the ICU was randomly assigned to either the dopamine or the norepinephrine group. The study drugs were continuously infused based on the dose that was calculated in terms of μg per kilogram per minute (μg/kg/min). The dose required to treat shock could be titrated to 20 μg/kg/min for dopamine and 0.2 μg/kg/min for norepinephrine. If a patient was assigned to the dopamine group, dopamine infusion was initiated, and the dose was titrated to 20 μg/kg/min. If a patient was assigned to the norepinephrine group, a continuous infusion of norepinephrine was initiated, and the dose was titrated to 0.2 μg/kg/min. Dose escalation for each study drug was determined by the

intensivists based on the severity of shock. If shock persisted despite the infusion of the maximal dose of a drug, second-line vasoactive inotropic agent infusion was initiated (epinephrine or vasopressin in the norepinephrine and norepinephrine in the dopamine group). A third-line agent (epinephrine or vasopressin) could be added if shock persisted despite the administration of second-line norepinephrine in the dopamine group. Once shock was observed to have resolved and the patient's vital signs had stabilized, the second-or third-line agents were weaned first, and then the study drugs were tapered based on the intensivist's decision. Patients who redeveloped shock during the same hospitalization were re-administered the previously assigned study drug first and then the second- and third-line drugs were added as described above. Other postoperative management was performed based on our CSICU protocol followed by the intensivist in charge.

The study drug infusion could be discontinued by the intensivist if any serious adverse events occurred.

End points

The primary outcome was the occurrence of newly developed arrhythmia (supraventricular, ventricular, or sinus tachycardia >120 beats per min [bpm]) while the patients were receiving the study drug infusion to treat shock. Secondary outcomes were 30-day all-cause mortality, requirement of a second- or third-line vasoactive drug, days free from vasoactive agents, length of hospitalization and ICU admission, and the composite outcome of postoperative complications within 30 days after study drug infusion.

Statistical analysis

The study performed by De Backer et al.[8] showed that the difference in the rate of arrhythmia caused by dopamine and norepinephrine was 12%. Based on this result, we calculated that 420 patients were required for enrollment to achieve 80% power at a two-sided alpha level of 0.05. Owing to the high hazard levels associated with the study, a sequential trial design was used. An interim analysis was preplanned after enrollment of the first 50 patients in each group. An independent statistician analyzed the data and adverse events and a futility boundary for the primary endpoint was crossed. The trial was discontinued following the

recommendation of the Safety Monitoring Committee.

Statistical analyses were performed based on the intention-to-treat principle. Intergroup differences were analyzed using the Mann–Whitney U test for continuous variables and the Fisher exact test for categorical variables. Comparison of the primary outcome was performed using the unadjusted chi-square test. Other outcomes were presented as odds ratios (OR) and 95% confidence intervals (CI) using logistic regression. All statistical analysis was performed using the SAS software version 9.3 (SAS Institute, Cary, NC, USA).

Results

Patient Characteristics

Of the 261 patients who were admitted to the ICU after cardiovascular surgery, 100 were enrolled as shown in Figure 1. Patients were randomly assigned to the dopamine (n=50) or the norepinephrine group (n=50) when shock persisted despite adequate fluid resuscitation. Baseline characteristics are summarized in Table 1 and were similar between the groups. Mean age was 57 years in the dopamine and 59 years in the norepinephrine group, and men comprised 62% of the study population. Most patients underwent valvular surgery or coronary artery bypass grafting (CABG). Operative characteristics were similar between the groups as shown in Table 2. Blood pressure and heart rate were stable at the time of ICU admission as summarized in Table 2. The first postoperative laboratory results obtained during ICU admission were also unremarkable in all patients.

Primary outcome

The primary endpoint of new onset arrhythmia was observed in 13 patients (13.2%) during the treatment of shock using the study drugs. Of these 13 patients, 12 belonged to the dopamine group. Sinus tachycardia with a heart rate >120 bpm occurred in 11 and atrial tachycardia in 1 patient. In the norepinephrine group, 1 patient showed sinus tachycardia (>120 bpm) (OR 16.3 95% CI 2.0–131.3, P=0.009). (Supplementary table 1) Atrial fibrillation occurred in 2 patients (4%) in the norepinephrine and 1 patient (2.1%) in the

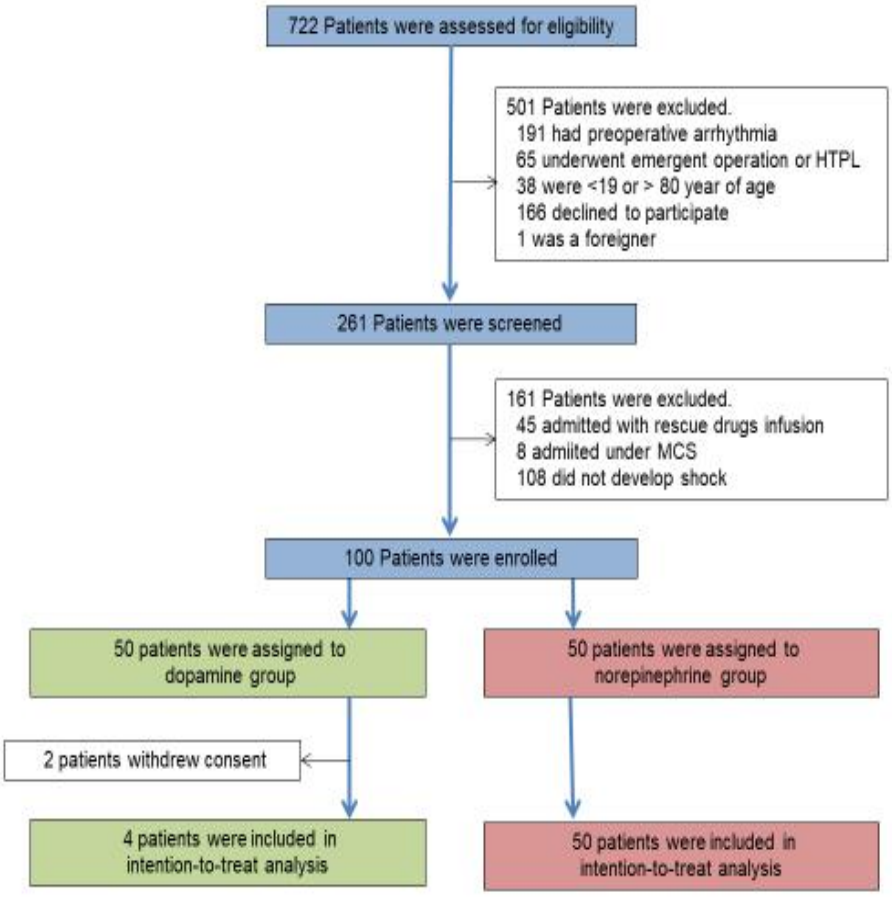

Fig.1 Screening and enrollment patients.

Table 1. Baseline characteristics of the patients

Variables	Dopamine (n=48)	Norepinephrine(n=50)	P value
Age, years	57.4 ± 15.2	59.3 ± 12.8	0.49
Sex (male), n (%)	30 (62.5)	32 (64.0)	0.33
Diabetes Mellitus, n (%)	8 (16.7)	10 (20.0)	0.87
Hypertension, n (%)	23 (47.9)	24 (48.0)	1.00
Cerebrovascular accident, n (%)	1 (2.1)	2 (4.0)	1.00
NYHA* 3,4, n(%)	8 (16.7)	11 (22.0)	0.28
Euro SCORE	2.1 ± 2.0	2.1 ± 3.6	0.98
LV‖ ejection fraction, %	58.8 ± 11.7	58.9 ± 10.8	0.98
Left atrial size, mm	39.9 ± 7.3	41.1 ± 7.6	0.96
Medication			
Angiotensin receptor blocker	8 (16.7)	7 (14.0)	0.93
Beta blocker	17 (35.4)	20 (40.0)	0.79
Calcium channel blocker	11 (22.9)	16 (32.0)	0.43
Statins	19 (39.6)	26 (52.0)	0.30
Antiplatelet	28 (58.3)	33 (66.0)	0.51
Laboratory			
Hemoglobin, g/dL	10.3 ± 1.3	10.2 ± 1.3	0.73
Creatinine, mg/dL	1.1 ± 1.4	0.8 ± 0.6	0.24
BUN**, mg/dL	14.6 ± 8.9	14.1 ± 4.4	0.71
Total bilirubin, mg/dL	1.1 ± 0.8	1.1 ± 0.6	0.87
Albumin, g/dL	2.7 ± 0.4	2.7 ± 0.4	0.60

Results are presented as mean ± SD, number (percentage).

*NYHA = New Yolk heart association; ‖LV = left ventricule; **BUN = blood urea nitrogen

Table 2. Operative and perioperative characteristics

Variables	Dopamine (n=48)	Norepinephrine(n=50)	P value
Type of operation			0.96
CABG	16 (33.3)	15 (30.0)	
Off-pump	11 (68.8)	9 (60.0)	
On-pump	5 (31.2)	6 (40.0)	
Valve	21 (43.7)	24 (48.0)	
CABG+valve	2 (4.2)	1 (2.0)	
Aorta	3 (6.3)	3 (6.0)	
Others	6 (12.5)	7 (14.0)	
CPB times, mins	117.8±54.3	131.1±92.3	0.47
ACC times, mins	76.9±46.5	46.5±69.9	0.27
APACHE II score	23.2 ± 5.4	24.5 ± 4.0	0.18
SOFA score	10.8 ± 2.2	11.2 ± 1.8	0.31
Vital signs at ICU admission			
Mean arterial pressure, mmHg	82.7 ± 12.6	85.0 ± 11.3	0.33
Heart rate, beats/min	84.6 ± 14.6	83.6 ± 12.3	0.72
Laboratory findings			
Arterial pH	7.4±0.05	7.4±0.05	0.85
$PaCO_2$, mmHg	35.9 ± 5.4	35.6 ± 4.9	0.71
PaO_2, mmHg	158.7 ± 77.1	172.8 ± 74.7	0.36
SaO_2, %	98.1 ± 1.8	100.2 ± 11.1	0.19
SvO_2, %	62.2 ± 9.7	62.5 ± 10.3	0.93
Lactate, mmol/L	1.8 ± 0.9	1.8 ± 0.8	0.68
Hemoglobin, g/dL	12.4 ± 2.0	13.2 ± 1.6	0.04
Creatinine, mg/dL	1.3 ± 1.7	2.2 ± 8.2	0.48
BUN, mg/dL	17.5±9.8	16.7±5.5	0.64
Total bilirubin, mg/dL	0.5±0.2	0.5±0.3	0.94
Albumin, g/dL	3.7±0.5	3.8±0.3	0.17

Results are presented as mean ± SD, number (percentage).

CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; ACC = aortic cross

clamp; APACHE = Acute Physiology and Chronic Health Evaluation; SOFA = sequential organ failure assessment; ICU = intensive care unit; BUN = blood urea nitrogen

dopamine group without the use of any vasoactive agents on postoperative day 1 and 2, respectively. Overall arrhythmic events were more common in the dopamine group, and this difference was statistically significant (OR 5.8, 95% CI 1.5–21.9, P=0.009).

Secondary outcomes

No in-hospital death or death during 30-day follow-up was reported. Regarding therapeutic interventions, second-line norepinephrine was administered to 37 patients (77.1%) in the dopamine group to elevate their blood pressure. Additionally, rescue drugs such as epinephrine and vasopressin were administered to 6 patients to treat persistent shock. Rescue drugs were administered to 4 patients (8.0%) in the norepinephrine group. Therapeutic interventions in addition to the administration of the study drugs to treat shock were more commonly required in the dopamine group as shown in Table 3 (OR 38.6, 95% CI 11.3–131.4, P<0.001). Postoperative complications occurred in 3 (10.0%) in the norepinephrine and 1 patient (2.1%) in the dopamine group, although this difference was not statistically significant. The mean length of ICU stay was 2.5 days in both groups. Length of hospitalization was also similar in both groups.

Discussion

In this single-blind randomized trial, we compared the efficacy of dopamine and norepinephrine in the treatment of post-cardiac surgery shock. Although no statistically significant difference was observed between the dopamine and norepinephrine groups in terms of the mortality rate, dopamine administration was significantly associated with tachyarrhythmic events. Furthermore, additional therapeutic interventions such as the use of rescue drugs were more commonly needed in the dopamine group to treat shock, and this intergroup difference was statistically significant. Postoperative myocardial infarction occurred in 1 patient undergoing CABG in the dopamine group because of sinus tachycardia (>120 bpm) during the study drug infusion. A tachycardia might contribute to myocardial ischemia by increasing the oxygen demand. Additionally, a high heart rate might also negatively affect the cardiac output by decreasing the stroke volume and the left ventricular filling time, which lead to hypotension and myocardial infarction. This finding was

Table 3. Outcomes between groups

Variables	Dopamine (n=48)	Norepinephrine *(n=50)	Odds ratio (95% CI)	P value
Arrhythmia on trial drugs, n (%)	12 (25.0)	1 (2.0)	16.3 (2.0-131.3)	0.009
Sinus tachycardia (>120bpm)	11 (22.9)	1 (2.0)		
Supraventricular tachycardia	1 (2.1)	0		
Arrhythmia, n (%)	13 (27.1)	3 (6.0)	5.8 (1.5-21.9)	0.009
Sinus tachycardia (>120bpm)	11 (22.9)	1 (2.0)		
Supraventricular tachycardia	2 (4.2)	2 (4.0)		
Therapeutic interventions,,	37 (77.1)	3 (6.0)	52.7 (13.7-202.7)	<0.001
Epinephrine, μg/kg/min	0.46±0.22	0.33±0.09		
Patients treated, n(%)	2 (4.2)	2 (4.0)		
Norepinephrine, μg/kg/min	3.11±2.53			
Patients treated, n(%)	37 (77.1)			
Vasopressin, μg/kg/min	0.29±0.27	0.43		
Patients treated, n(%)	4 (8.3)	1 (2.0)		
Dobutamine, μg/kg/min	23.3±6.23			
Patients treated, n(%)	23 (47.9)	10 (20.0)		
Vasopressor free duration, days	28.7±1.00	28.7±1.05		
Dose to treat shock,μg/kg/min	50.6±45.8	0.56±0.62		
Length of ICU stay, days	2.5 ± 2.6	2.5 ± 4.7		
Length of hospital stay,days	11.2 ± 10.3	9.9 ± 9.9		
Complications	0	3 (10.0)		
Re-exploration, n (%)	0	2 (4.0)		
Stroke, n (%)	0	2 (4.0)		
MCS, n (%)	0	0		
Prolonged ventilation, n (%)	0	1 (2.0)		
In-hospital mortality, n (%)	0	0		
30-day mortality, n (%)	0	0		

Results are presented as mean ± SD, number (percentage).

*; reference value for logistic regression. MCS = mechanical circulatory support

consistent with a previous study performed by De Backer et al.[8] which demonstrated that dopamine was associated with a greater occurrence of arrhythmic and ischemic events with similar 28-day mortality in the entire cohort. However, subgroup analysis showed that the mortality rate among patients with cardiogenic shock was higher in the dopamine group. A recent meta-analysis[10] that compared between dopamine and norepinephrine for the treatment of cardiogenic shock also demonstrated that dopamine was associated with higher 28-day mortality, as well as a higher risk of arrhythmic events regardless of whether the cardiogenic shock was secondary to coronary heart disease or other etiologies. However, our study failed to demonstrate a significant intergroup difference in the mortality rate. Arrhythmia spontaneously resolved in all patients after discontinuation of the study drugs, and shock was appropriately treated with the administration of second- or third-line vasoactive drugs. Therefore, no death was reported in either group in our study.

Arrhythmia is a common complication after cardiac surgery and contributes to considerable morbidity and mortality. Atrial tachyarrhythmias are more common than ventricular tachyarrhythmias or bradyarrhythmia.[11] Reportedly, the incidence of atrial fibrillation (the most common supraventricular tachyarrhythmia) was 15–40% after CABG and approximately 60% in those undergoing valve replacement concomitant with CABG.[12,13] Although the pathomechanism of postoperative tachyarrhythmias has not been clearly understood, inflammatory mechanisms occurring after cardiac surgery, hemodynamic stress, ischemic injury during cardiopulmonary bypass and aortic cross-clamping or CABG are considered contributory factors.[14-16] In our study, ventricular tachyarrhythmia or bradyarrhythmia was not reported in any patient. All arrhythmias observed in our study were tachyarrhythmias with an incidence of approximately 16% among all patients. Most arrhythmias developed during the infusion of dopamine to treat shock, and this finding was consistent with a previous report that has suggested that dopamine was associated with dose-related sinus tachycardia.[17] Regarding the type of surgery, CABG may be one of the contributory factors aggravating myocardial ischemic injury. In our study, CABG was associated with arrhythmic events with marginal significance (P=0.07). Postoperative atrial fibrillation was observed to be associated with increased mortality in patients undergoing CABG.[18,19] Therefore, the administration of pro-arrhythmic agents such as dopamine should

be avoided in the postoperative period after CABG.

Limitations of our study: 1) Our study was a single-blind and not a double-blind trial, which by itself might serve as a potential confounder. 2) The number of patients enrolled in this study was small. During the interim analysis after the enrollment of the first 50 patients out of 210 patients calculated in each group, adverse events and a futility boundary for the primary endpoint was crossed, and the trial had to be discontinued. This might mean that the pro-arrhythmic adverse effect of dopamine compared with norepinephrine was significant enough to prove a statistical difference despite the small number of patients studied. 3) Dopamine and norepinephrine differ in terms of their pharmacological effects. Despite being a less potent vasopressor, dopamine was considered equipotent to norepinephrine. Thus, dose escalation of the study drugs was performed within the same therapeutic range. This might have contributed to the fact that those receiving dopamine required the administration of additional vasoactive agents to treat shock. 4) We enrolled patients undergoing cardiovascular surgery to ensure that the study population was more homogeneous; however, among these patients, etiologies necessitating cardiovascular surgery varied from valvular disease to aortic disease. The differences in these underlying etiologies and the different types of surgeries performed might serve as another confounder, although the type of surgery performed between groups was similar.

Conclusions

Compared with norepinephrine, dopamine significantly increased the occurrence of arrhythmic events in patients with post-cardiac surgery shock. Moreover, the requirement of additional vasoactive agents to treat shock was higher in the dopamine group. A further study with a larger cohort may be necessary to accurately determine optimal vasoactive inotropes inotropic or vasoactive agents to treat post-cardiac surgery shock.

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Appendix

Supplementary table 1. Characteristics of the patients undergoing tachy-arrhythmic events during trial drug infusion

No.	Random	Age	Sex	Euro SCORE	EF(%)	Name of operation	Arrhythmia	Dose to treat shock*	Additional vasoactive drugs to treat shock
1	D	33	M	1.29	64	MVR	AT	5	N
2	D	74	F	2.14	62	AVR	ST	43	N
3	D	48	M	0.55	55	CABG	ST	74	
4	D	71	F	2.60	71	OPCAB	ST	78	N, V
5	D	71	M	7.50	58	PVR	ST	3	N, Epi, V
6	D	61	F	0.64		OPCAB	ST	10	N
7	D	59	M	1.10	38	CABG	ST	7	N, V
8	D	60	M	1.06	66	OPCAB	ST	6	N
9	D	35	M	0.96	59	Asc., hemiarch replacement	ST	10	N
10	D	38	M	1.46	50	Bentall's operation	ST	2	N
11	D	66	M	1.76	48	OPCAB	ST	21	N
12	D	73	M	1.16	71	Sutureless AVR	ST	12	N, Epi, V
13	N	53	M	3.64	11	OPCAB	ST	3.5	Epi

* μg/kg/min, EF = ejection fraction; D = dopamine; M = male; MVR = mitral valve replacement; AT = atrial tachycardia; N = norepinephrine; AVR = aortic valve replacement; ST = sinus tachycardia; F = female; CABG = coronary artery bypass grafting; OPCAB = off pump coronary artery bypass; V = vasopressin; PVR = pulmonic valve replacement; Epi = epinephrine; Asc = ascending aorta

연구배경: 심장 수술 후 다양한 원인에 의한 쇼크가 드물지 않게 발생하게 되는데 쇼크는 생명에 위협이 되는 상태이기 때문에 치료를 위해서는 수액 공급과 적절한 강심제의 사용이 매우 중요하다. 하지만 어떤 종류의 강심제가 심장 수술 후 발생한 쇼크의 치료에 가장 효과적인지는 근거도 희박하고 정립되지 않은 상태이다. 따라서 본 연구는 심장 수술 후 발생한 쇼크의 치료로서 dopamine 과 norepinephrine 의 효과를 비교하고자 한다.

연구방법: 심장 수술 후 쇼크가 발생한 환자들을 1 차 약물로서 dopamine 군 과 norepinephrine 군에 무작위 배정하여 전향적인 연구를 진행하였다. 연구약물의 최고용량 (dopamine 20 mcg/kg/min, norepinephrine 0.2 mcg/kg/min) 에도 불구하고 쇼크가 지속되거나 연구약물 사용 도중 빈맥성 부정맥이 발생하여 연구약물을 중단해야 하는 경우 2 차 약물 (epinephrine and vasopressin)을 사용하여 쇼크를 치료하도록 하였다. 1 차 연구 종료점은 연구약물 사용 도중 새롭게 발생한 빈맥성 부정맥 (supraventricular, ventricular, or sinus tachycardia)이었다. 2 차 연구종료점은 모든 원인의 조기 사망 (30 일), 재원기간, 중환자실 재원기간, 조기합병증, 그리고 2 차약물의 사용 등이었다. 각 군에 210 명씩, 총 420 명 (80% power at a two-sided alpha level of 0.0)을 등록하도록 설계하였고, 각 군에 첫 50 명이 등록된 시점에서 중간 분석을 시행하여 연구의 안전성을 검증하기로 하였다.

연구결과: 총 100 명이 등록된 시점 (dopamine 군 48 명, norepinephrine 군 50 명, 2 명 탈락)에서 중간 분석을 시행하였고 연구의 1 차 연구 종료점인 부정맥의 발생에 있어 두 군 간에 유의한 차이가 있어 더 이상의 연구를 진행하지 않고 연구를 종료하였다. 두 군 간의 환자 특성은 비슷하였다. 하지만 dopamine 군에서 12 명의 환자에서 빈맥성 부정맥이 발생한 반면, norepinephrine 군에서는 1 명의 환자에서 빈맥성 부정맥이 발생하여 양군에 유의한 차이가 있음을 알 수 있었다. (odds ratio [OR] 16.3, 95% confidence interval [CI], 2.0–131.3, P=0.009). 또한 쇼크를 치료하기 위한 2 차 약물의 사용이 dopamine 군에서 유의하게 높았다. (OR 52.7, 95% CI 13.7–202.7, P<0.001). 그 외에 2 차 연구 종료점은 양군 간에 큰 차이가 없었다.

결론: 심장 수술 후 발생한 쇼크의 치료로서 dopamine 의 사용은 norepinephrine 에 비해 빈맥성 부정맥의 발생을 증가시킬 뿐 아니라, 쇼크를 치료하기 위해 추가적인 승압제의 사용 빈도가 높았다.