

The comparison of monitored anesthesia care with dexmedetomidine and spinal anesthesia during varicose vein surgery

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Purpose: The purpose of this study was to investigate the effectiveness and safety of monitored anesthesia care (MAC) using dexmedetomidine for its sedative and analgesic effect during varicose vein surgery.

Methods: Forty-two patients, who underwent varicose vein surgery, were divided into the MAC group (n = 20) or the spinal anesthesia group (n = 22) for randomized clinical trial. In the MAC group, dexmedetomidine was administered by a loading dose of 1 µg/kg for 10 minutes, followed by a maintenance infusion of 0.2-1.0 µg/kg/hr. Ketamine was used for intermittent injection. In the spinal anesthesia group, midazolam was used for sedation. Intraoperative vital signs, the number of adverse events, and the satisfaction of patients and surgeons concerning the anesthetic condition were compared between the two groups.

Results: Systolic blood pressure was intraoperatively significantly different over time between the two groups. The groups had statistical differences in the change in heart rate with regard to time. In the postanesthetic care unit, patients and surgeons in the MAC group had a lower satisfaction score, compared to patients and surgeons in the spinal anesthesia group. However, in the recovery period, patients had a positive perception concerning MAC anesthesia. In addition, without significant adverse events, the MAC group had a shorter time to possible ambulation, which indicated an early recovery.

Conclusion: We believe that MAC using dexmedetomidine in combination with ketamine may be an alternative anesthetic technique for varicose vein surgery with regard to a patient's preference and medical condition.

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Key Words: Dexmedetomidine, Monitored anesthesia care, Sedation, Spinal anesthesia

INTRODUCTION

A significant number of varicose vein surgeries have been performed under regional anesthesia or general anesthesia. The advantages of using regional anesthesia are that patients mostly cannot feel pain and surgeons are not interrupted by the motion of a patient's lower extremities during the

surgery. However, complications may be occurred such as numbness, postdural puncture headache, nausea, vomiting, or extended time to ambulation. For many patients under regional anesthesia, a sedative agent is also needed because of a patient's anxiety, nervousness, and intolerable response concerning surgical ambience. Monitored anesthesia care (MAC) is performed without regional anesthesia to improve the

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patient's postoperative condition in vascular procedures. The most commonly used agents for MAC are midazolam, propofol, and fentanyl [1-3]. It is well known that a combination of these drugs is often difficult to titrate and may induce respiratory depression.

Dexmedetomidine, a highly selective α -2 receptor agonist, acts as a sedative, sympatholytic, and anxiolytic. It was introduced for the patients whose trachea was intubated in the intensive care unit [4]. Since its introduction, dexmedetomidine has been used as a sedative and hypnotic agent for patients who do not need tracheal intubation. Dexmedetomidine reportedly has been used successfully as the primary sedative in a broad variety of surgical and diagnostic procedures performed under MAC [5-8]. It enables patients to respond to verbal stimuli during surgery, but without significant respiratory depression [9,10]. Several reports have proven that dexmedetomidine has advantages such as a narcotic sparing effect, sympatholysis, analgesia, and greater patient satisfaction.

We therefore decided to investigate whether a MAC method using dexmedetomidine combined with ketamine alone could provide sufficient effective sedation and hemodynamic stability so that varicose vein surgery can be conducted. We present the results of a prospective randomized clinical trial that evaluated the efficacy and safety of dexmedetomidine with ketamine under MAC, compared with spinal anesthesia, in patients undergoing varicose vein surgery.

METHODS

This study was a prospective, randomized controlled trial. Patients were scheduled for elective varicose vein surgery, which was performed in an operating room under MAC or under spinal anesthesia. Varicose vein surgery comprised radiofrequency ablation with local anesthetic infiltration and phlebectomy. There was no premedication. All surgery was performed over 30 minutes within 2 hours. Eligible patients were at least 20 years to at most 70 years and had an American Society of Anesthesiologists physical status of 1-2. We received from all patients written informed consent forms that explained to them the object of the clinical study. Patients were excluded if they had undergone general anesthesia within 7 days; had taken an α -2 agonist within 14 days; had experienced acute unstable angina or myocardial infarction within the previous 6 weeks; had bradycardia with a heart rate (BP) less than 50 beats per minute; had a systolic blood pressure (SBP) less than 90 mmHg; were pregnant, had third degree heart block, had the contraindication of neuraxial block; or the patient refused. On arriving at the operating room, patients were monitored by noninvasive blood pressure, electrocardiography, pulse oximetry, and bispectral index (BIS). Vital signs were recorded every 5 minutes throughout the procedure. BIS was only

restricted monitoring for understanding the sedation status of patients due to arising of BIS score in case of using ketamine.

Oxygen (3 L/min) was supplied by nasal oxygen cannula. We evaluated the incidence of adverse events such as hypotension (i.e., a SBP less than 90 mmHg and less than 70% of baseline); hypertension (i.e., a SBP greater than 160 mmHg and 130% of the baseline); bradycardia (i.e., a heart rate [HR] less than 50 bpm); tachycardia (i.e., a HR greater than 120 bpm); hypoxia (i.e., an oxygen saturation [SpO₂] less than 93%); nausea; vomiting; or shivering. When adverse events occurred, we used intravenous nicardipine (1 mg; for hypertension), ephedrine (5 mg; for hypotension), atropine (0.5 mg; for bradycardia), esmolol (20 mg; for tachycardia), and assisted ventilation with oxygen supply (for hypoxia).

Patients were randomly divided into two groups: dexmedetomidine with ketamine under MAC (i.e., the MAC group) or spinal anesthesia with midazolam (i.e., the SA group). In the MAC group, a loading dose of 1 μ g/kg of dexmedetomidine was administered over 10 minutes, which was followed by a maintenance infusion beginning at a rate of 0.6 μ g/kg/hr. Every 5 minutes, the sedation state was assessed by the observer's assessment of alertness/sedation score (OAA/S; Table 1) and the infusion rate of the drug was titrated 0.2-1.0 μ g/kg/hr to maintain an OAA/S score of 4 or less throughout the surgery. It was not until the OAA/S score was 4 or less that the procedure was started. For reducing the pain response, we used ketamine 2 times intravenously. At 1 minute before the radiofrequency catheterization, we administered 0.6 mg/kg of ketamine. At 1 minute before the phlebectomy, the second dose (at the same dosage) of ketamine was injected. The infusion of dexmedetomidine was stopped at the beginning of the elastic band dressing.

In the SA group, we performed spinal anesthesia using 13-15 mg of 0.5% bupivacaine, which was injected intrathecally by a midline or paramedian approach at the L3-4 or L4-5 interspace using a 25-gauge Quincke spinal needle. After 15 minutes of injecting intrathecal local anesthetic drugs, 0.05 mg/kg of midazolam was administered intravenously. After 15 minutes, 0.5 mg of midazolam was added if the OAA/S score was greater than 4.

The recorded vital signs in the operating room were com-

Table 1. Observer's assessment of alertness/sedation scale

Definition	Score
Responds easily to name spoken in a normal tone	5
Responds only after mild prodding or shaking	4
Responds only after name is called loudly and/or repeatedly	3
Lethargic response to name spoken in normal tone	2
Does not respond to mild prodding or shaking	1

pared at the following times: T1, baseline; T2, 5 minutes after the loading of dexmedetomidine in the MAC group or 5 minutes after performing intrathecal local anesthetic injection in the SA group; T3, 5 minutes after T2; T4, 5 minutes after T3 (i.e., 5 minutes after the maintenance infusion of dexmedetomidine in the MAC group); T5, 5 minutes after T4 (i.e., 5 minutes after the injection of midazolam in the SA group); T6, 5 minutes after injection of first dose of ketamine in the MAC group or 5 minutes after T5 in the SA group; T7, 5 minutes after T6; T8, at the end of surgery. The same steps in the varicose vein surgery were performed at approximately each compared time in the two groups.

After confirming the successful induction of MAC or spinal anesthesia, the overall course of surgery was as follows. After the incision of the skin, an angiocatheter was used under the ultrasound guidance to puncture the side of the lesion of the great saphenous vein (GSV). A guide-wire was passed into the GSV. This was followed by the insertion of a 7-French sheath. Once the 7-French sheath was in place and confirmed by ultrasound, a 7-French 60-cm radiofrequency catheter was inserted and positioned 2 cm from saphenofemoral junction. With the catheter in place and secured at this level, a 0.5% solution of lidocaine with normal saline was used to create tumescent local anesthesia to compress the GSV along the course of the radiofrequency catheter. Serial puncture wounds were visualized with ultrasound to ensure the delivery of the tumescent solution adjacent to the vein, the compression of the vein, and the removal of the vein from its surface location to a deeper location for the radiofrequency ablation. With tumescent local anesthesia completed, the endovenous catheter was then used to perform radiofrequency ablation of the entire great saphenous segment of the thigh down to the level of the knee joint for GSV. After completing the ablation procedure, deep

vein thrombosis and complete ablation of saphenous trunk were evaluated by ultrasound examination. The catheter was removed and a serial stab phlebectomy was performed. Areas of the phlebectomies were reapproximated with quarter-inch Steri-Strips. The leg was then wrapped with 2 layers of elastic compression stocking. In both groups, the entire anesthetic and operating time were similar.

After completing the surgery, the patients remained in the postanesthetic care unit (PACU). Vital signs were recorded every 5 minutes for the first 15 minutes, and then recorded every 15 minutes for 45 minutes. The OAA/S score and verbal numerical rating scales of pain from 0 (no pain) to 10 (worst pain) were assessed while patients recovered in the PACU.

To compare the efficacy and safety of MAC using dexmedetomidine with those of spinal anesthesia with midazolam, we also recorded the incidence of hypotension, hypertension, bradycardia, tachycardia, shivering, nausea, and vomiting during the procedure. We evaluated the satisfaction of the anesthetic condition during the surgery from the viewpoint of the surgeons and the patients in the PACU (based on a verbal rating scale from 0 [worst] to 10 [best]). The following day, the patients were visited to assess their overall level of satisfaction with their anesthetic type. They were assessed by the Iowa Satisfaction with Anesthesia Scale (ISAS) [11] (Table 2). By using the questionnaire, we recorded the time to ambulation after surgery, symptoms of postoperative nausea, vomiting, postdural puncture headache, numbness, recall of perioperative events, and intention to have the same anesthesia again for the next opportunity.

All results are expressed as the mean (standard deviation). The demographic data of the patients, parametric data, satisfaction, and the pain score between two groups were analyzed by using the Student t-test. Repeated measures analysis of variance and a multicomparative test were used to compare the hemodynamic changes in each group over time. The frequency of adverse events was determined by the Fisher exact test. The ISAS was compared by the Mann-Whitney U test.

Table 2. Patient assessment from ISAS

1. I threw up or felt like throwing up.
2. I would have the same anesthetic again.
3. I itched.
4. I felt relaxed.
5. I felt pain.
6. I felt safe.
7. I was too hot or cold.
8. I was satisfied with the anesthetic care.
9. I felt pain during surgery.
10. I felt good.
11. I hurt.

For items 1, 3, 5, 7, 9, and 11, the scores are calculated as follows: +3, agree very much; +2, agree moderately; +1, agree slightly; -1, disagree slightly; -2, disagree moderately; -3, disagree very much. For items 2, 4, 6, 8, and 10, the scores are calculated in the reverse order from the aforementioned items. A higher score indicates a more favorable outcome. ISAS, Iowa Satisfaction with Anesthesia Scale.

Table 3. Patient demographic characteristics

Characteristic	MAC group (n = 20)	SA group (n = 22)
Age (yr)	51.0 (15.5)	53.1 (12.3)
Height (cm)	168.2 (9.2)	167.7 (9.3)
Weight (kg)	69.3 (7.3)	70.5 (10.7)
Gender		
Male/female	13/7	14/8
ASA physical status		
1/2	12/8	11/11

Values are presented as the mean (standard deviation) or patient number.

ASA, American Society of Anesthesiologists; MAC, monitored anesthesia care; SA, spinal anesthesia with midazolam.

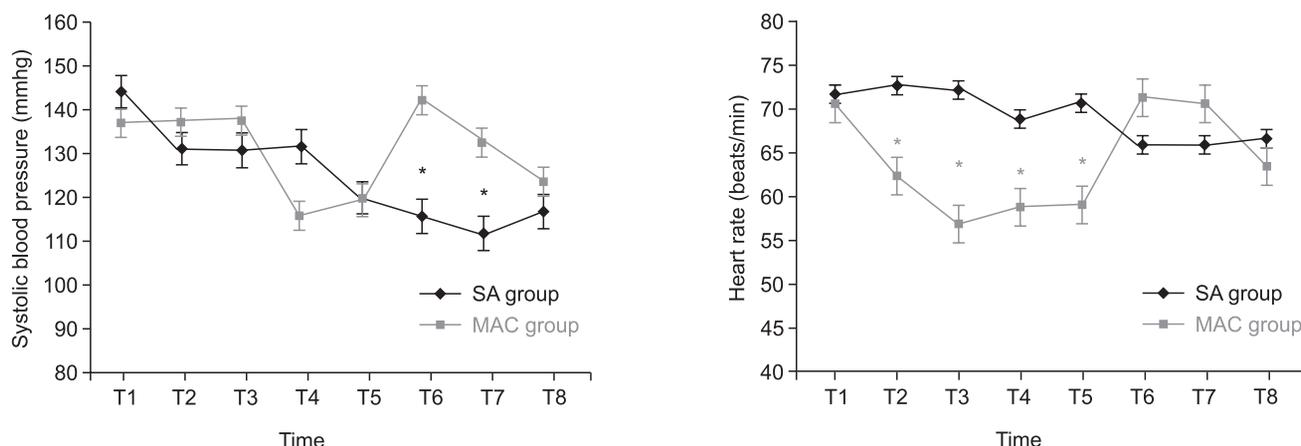


Fig. 1. Changes in hemodynamic variables. MAC, monitored anesthetic care with dexmedetomidine; SA, spinal anesthesia; T1, baseline; T2, 5 minutes after loading of dexmedetomidine in the MAC group, or 5 minutes after performing intrathecal local anesthetic injection in the SA group; T3, 5 minutes after T2; T4, 5 minutes after T3 (5 minutes after maintenance infusion of dexmedetomidine in the MAC group); T5, 5 minutes after T4 (5 minutes after injection of midazolam in the SA group); T6, 5 minutes after injection of first dose of ketamine in the MAC group, or 5 minutes after T5 in the SA group; T7, 5 minutes after T6; T8, at the end of surgery. * $P < 0.05$, the MAC group vs. the SA group.

Statistical analyses were performed using PASW Statistics ver. 18.0 (SPSS Inc., Chicago, IL, USA). Findings with a P-value of less than 0.05 were considered significant.

RESULTS

Of 42 patients, 20 patients were randomized to the MAC group and 22 patients were randomized to the SA group. Table 3 presents the characteristics of the subdivided groups. There were no significant differences between the groups.

Fig. 1 presents changes in the hemodynamic variables. There was no significant difference in the initial SBP between the two groups (137.4 ± 18.7 mmHg for the MAC group and 144.4 ± 19.6 mmHg for the SA group) ($P = 0.412$). However, the SBP showed a significant difference over time between the two groups ($P = 0.011$). At T6, the SBP was significantly higher in the MAC group at 5 minutes after the infusion of ketamine (142.6 ± 26.0 mmHg) than in the SA group at 10 minutes after the injection of midazolam (116.0 ± 13.6 mmHg) ($P = 0.008$). At T7, there was a significant difference between the MAC group (133.0 ± 22.7 mmHg) and the SA group (112.3 ± 8.8 mmHg) ($P = 0.02$). In the MAC group, the injection of low-dose ketamine attenuated the dexmedetomidine-induced decrease in the SBP. On the other hand, the SBP remained lower than the baseline during the overall procedure in the SA group.

There was statistical difference over time between the groups in the change in HR ($P = 0.029$). From T2 to T5, the MAC group had a significantly lower pulse rate in comparison to the SA group ($P = 0.002$ [T2]; $P = 0.000$ [T3]; $P = 0.003$ [T4]; and $P = 0.001$ [T5]). However, there was no significant difference between the two groups after the injection of ketamine in the

Table 4. Distribution of adverse events during operation

Adverse event	MAC group	SA group	P-value
Hypotension	6 (30)	9 (40.9)	0.659
Hypertension	4 (20)	0 (0)	0.035*
Bradycardia	2 (10)	0 (0)	0.214
Tachycardia	0 (0)	0 (0)	
Hypoxia	0 (0)	0 (0)	
Nausea or vomiting	0 (0)	1 (4.5)	1.000
Shivering	0 (0)	1 (4.5)	1.000

Values are presented as number (%).

MAC, monitored anesthesia care; SA, spinal anesthesia with midazolam.

* $P < 0.05$, the MAC group vs. the SA group.

MAC group. The respiratory rate and SpO_2 were comparable between the two groups. Neither group had episodes of respiratory depression or oxygen desaturation.

Adverse events are summarized in Table 4. The overall number of adverse events (e.g., hypotension, bradycardia, tachycardia, hypoxia, nausea, vomiting, or shivering) was similar between the groups; however, the incidence of hypertension was higher in the MAC group.

In the PACU, there was no statistically significant difference between the two groups with regard to the SBP ($P = 0.213$) or HR ($P = 0.289$). There were no reduced SpO_2 events or other respiratory complications in either group. In addition, from immediately after the completion of surgery until discharge from the PACU, the patients' verbal pain scores (VPSs; ranging from 0 [no pain] to 10 [worst pain]) were not significantly different between the two groups ($P = 0.316$). The overall VPS was higher in the MAC group than in the SA group, although

Table 5. Satisfaction of survey results

	MAC group	SA group	P-value
Patient's satisfaction ^{a)}	7.4 (1.7)	9.0 (0.9)	0.018*
Surgeon's satisfaction ^{a)}	6.2 (1.8)	9.1 (0.6)	0.001*
Overall ISAS score ^{b)}	11.4	10.6	

Values are presented as the mean (standard deviation) or mean value.

MAC, monitored anesthesia care; SA, spinal anesthesia with midazolam; ISAS, Iowa Satisfaction with Anesthesia Scale.

^{a)}The verbal rating scale (0 [worst] to 10 [best]), which was recorded in the postanesthetic care unit. ^{b)}The mean value, which was recorded on the day after surgery.

*P < 0.05, the MAC group vs. the SA group.

the VPS recorded at 15 minutes after a patient's arrival at the PACU was 4 or less on 90% of occasions.

Table 5 shows the satisfaction results. When the results were recorded in the PACU, the patients' and surgeons' satisfaction scores were lower in the MAC group. Surgeons especially showed a greater difference between the two groups. However, the mean value of the postoperative ISAS—evaluated on the day after surgery—was 11.4 in the MAC group and 10.6 in the SA group; there was no significant difference (P = 0.809). This indicates that in the recovery period, patients in the MAC group and the SA group may be similarly satisfied with their experience with the anesthetic condition.

In the recovery data analysis (Table 6), the MAC group had a shorter time to possible ambulation, compared to the SA group (P = 0.002). This indicates that MAC makes it possible for patients to recover and walk without assistance more quickly. Therefore, it shortens the duration of the hospital stay, and patients feel more comfortable with a rapid return to social activities. In addition, a considerable number of patients in the MAC group and in the SA group intended to have the same anesthesia at the next opportunity.

DISCUSSION

Our results in this study suggest that dexmedetomidine is an effective and safe drug when combined with ketamine for MAC of patients undergoing varicose vein surgery. Dexmedetomidine, a highly selective α -2 adrenoceptor agonist, produces sedation and anxiolysis and inhibits sympathetic activity. Dexmedetomidine has been used in the intensive care unit for critically ill patients who have mechanical ventilatory support. Dexmedetomidine has recently been used as the primary sedative drug during orthostatic surgery, ophthalmic surgery, dental surgery, and plastic surgery, and during diagnostic procedures such as fiberoptic bronchoscopy or gastrointestinal endoscopy [5-8,12].

Dexmedetomidine has an advantage in that it does not

Table 6. Recovery data

Variable	MAC (n = 20)	SA (n = 22)	P-value
Time of possible ambulation (hr), mean (SD)	4.8 (1.39)	7.9 (2.30)	0.002*
Intention to have same anesthesia	18 (90.0)	16 (72.7)	
Nausea or vomiting	4 (20.0)	2 (9.1)	
Recall about pain during surgery	2 (10.0)	0 (0)	
Amnesia at post anesthetic care unit	11 (55.0)	14 (63.6)	

Values are presented as number (%) unless otherwise indicated. MAC, monitored anesthesia care; SA, spinal anesthesia with midazolam; SD, standard deviation.

*P < 0.05, the MAC group vs. the SA group.

cause respiratory depression; this is because it is not mediated by the γ -aminobutyric acid system [13]. For that reason, dexmedetomidine sedation has been used safely in patients with compromised airways and during difficult airway fiberoptic intubation to preserve respiration [14,15]. Apan et al. [16] showed that compared to midazolam, dexmedetomidine allows a more stable intraoperative HR and less postoperative pain; they therefore report that MAC using dexmedetomidine is an appropriate agent for cataract surgery. Rich [17] reported that dexmedetomidine used in conjunction with local anesthesia provided adequate sedation for a patient with a complicated medical history and difficult-to-manage airway who underwent axillofemoral bypass graft. According to Huncke et al. [18], dexmedetomidine is a safe and effective sedative with an anesthetic sparing effect and may be a useful agent for patients undergoing vascular procedures.

Dexmedetomidine infusion causes a dose-dependent decrease in blood pressure and HR, which occur by a decreased concentration of plasma norepinephrine. The baroreceptor reflex and enhanced vagal activity are partly associated with this hemodynamic change, in addition to a decrease in sympathetic outflow and circulating catecholamine levels. In several studies, using a loading dose of dexmedetomidine reportedly induces cardiovascular depression. According to Bloor et al. [19], dexmedetomidine administered at a rate of 0.25–2.0 μ g/kg for 2 minutes reduces arterial pressure and cardiac output, although large doses of dexmedetomidine (1 μ g/kg or 2 μ g/kg) produces a temporary initial increase in the arterial pressure, presumably because of peripheral vasoconstriction. Despite concerns of cardiovascular depression, we performed the loading of dexmedetomidine for more rapid sedation, and added ketamine to oppose the cardiovascular depressant effect of dexmedetomidine.

Varicose vein surgery is relatively less invasive and takes a short time, but it is accompanied by painful surgical stimuli when performing catheter insertion, radiofrequency ablation,

and phlebectomy. Therefore, we used a loading dose of dexmedetomidine, followed by a continuous infusion that was adjusted (based on the OAA/S score) during the operation by adding low-dose ketamine just before initiating painful procedures to control pain and to supply appropriate sedative states for deeper conscious sedation. The hypotensive and bradycardic effects of dexmedetomidine were opposed by the indirect stimulatory effects of ketamine [20]. Therefore, severe hypotension and bradycardia in our study did not occur intraoperatively or postoperatively. We did not demonstrate intraoral dryness, although increased salivation associated with ketamine could be attenuated by the potent antisialogogue effect of dexmedetomidine. Scher and Gitlin [21] reported that they performed successful fiberoptic intubation under adequate sedation with dexmedetomidine and low-dose ketamine with clear secretions. In addition, ketamine has the advantages of minimal impact on the ventilatory drive and analgesic properties.

Because dexmedetomidine is a weak amnestic agent, the coexisting infusion of ketamine may have contributed to the partial amnesia. In our study, amnesia in patients was not statistically different between the two groups, and it affected more than 50% of patients. The OAA/S showed that even using low-dose ketamine to provide more profound sedation did not delay discharge from the PACU.

Dexmedetomidine attenuates drug-induced delirium [22]. The combined use of benzodiazepines and opioids has the potential risk of producing delirium; however, dexmedetomidine reportedly can minimize delirium in elderly patients [23]. That is the reason that dexmedetomidine could be used as a sedative in patients with a high risk of delirium. In addition, dexmedetomidine has advantages such as a short half-life that enables titration to the desired effect via an intravenous infusion, rapid onset, rapid recovery avoiding hangover effects, and the production of mild analgesia [24]. Dexmedetomidine potentiates the analgesic effect through their action at central and peripheral sites. It has an analgesic sparing effect through disinhibition of the noradrenergic nuclei by the inhibition of the locus ceruleus [25]. By preventing norepinephrine release, α -2 adrenergic receptors located at nerve endings may be involved in the analgesic effect. Goksu et al. [26] revealed that dexmedetomidine, when used for intraoperative anesthesia, has a sufficient analgesic effect and surgical comfort for patients undergoing functional endoscopic sinus surgery under local anesthesia.

Spinal anesthesia causes near complete analgesia during surgery, although it can cause side effects such as hypotension, bradycardia (caused by sympathetic blockade), nausea, vomiting, and sometimes shivering. For sedation, additional sedative drugs may need to be combined; therefore, we used midazolam. In our study, both anesthesia methods were safely performed

without any serious complications during or after the operative period. Therefore, for patients without any particular underlying disease, it is advisable to select an anesthetic method that is based on the preference of the patient.

In the subjective satisfaction score (measured by the ISAS), the MAC group was not statistically significantly different from the SA group. Dexmedetomidine enables a patient to transition easily and comfortably between the sedation state and the cooperative state. Dexmedetomidine provides an anxiolytic effect to patients under MAC. In this condition, patients can be relieved of the fear of spinal needle insertion, the feeling of paralysis, and the numbness that occurs with spinal anesthesia.

We checked surgeons' satisfaction in the PACU. Unlike the patients' ISAS score, surgeons expressed less satisfaction under MAC because of the leg motions and meaningless words spoken by patients during surgery. The reason may be that ketamine used for deeper sedation for surgical pain made it difficult for patients to be cooperative during sedation.

Spinal anesthesia has a relatively high incidence of side effects, early recovery times are longer, and the most troublesome complications of spinal anesthesia are related to residual effects of the block on motor, sensory, and sympathetic nervous system function. These residual effects can contribute to delayed ambulation, dizziness, urinary retention, and impaired balance. Compared to spinal anesthesia, MAC-based techniques have the advantages of facilitating recovery and of shortening the time to ambulation, time to oral intake, time to home-readiness, and duration of hospital stay. MAC is more cost effective and can enhance patient satisfaction because it facilitates an earlier resumption of normal activities of daily living, including returning to work.

There are some limitations to this study. The primary limitation of our study was comparing MAC to spinal anesthesia. It may be that spinal anesthesia offers near complete analgesia and motor blockade so that it can promote a superior surgical condition, compared to MAC. Surgeons may have been able to detect which patients were receiving spinal anesthesia through the patients' response during surgery. Because of differences in the induction technique between the two anesthetic methods, patients can also realize which anesthetic method is applied. The blinding of the treatment arm consequently could not be accomplished among patients or among surgeons. This may have biased the results.

Another limitation was the comparison of hemodynamic variables because it is difficult to determine a comparable time between the two groups based on the different infusion time of each sedative agent. Therefore, we tried to analyze the profiles by adjusting at the beginning of the anesthetic treatments and by using nearly the same surgical procedure. However, this also may have influenced the results.

In conclusion, we believe that dexmedetomidine is a safe

and effective sedative agent, and it seems to be an acceptable agent when added to low-dose ketamine for MAC in patients undergoing varicose vein surgery. Based on this study, we anticipate that low-dose ketamine can compensate for the hemodynamic effects of dexmedetomidine. Compared with spinal anesthesia combined with midazolam, MAC using dexmedetomidine and ketamine showed a compatible stable hemodynamic profile during the period of operation. In the MAC group, the adverse events were minimal, recovery time was shorter, and patient satisfaction was comparable. In addition, MAC using dexmedetomidine is a good alternative when patients undergoing varicose vein surgery have difficult

factors for spinal anesthesia such as coagulopathy, other bleeding diathesis, preexisting neurological deficits, definite patient refusal, or severe spine deformity. However, future studies will need to improve the quality of MAC such as avoiding the intraoperative motion of patients, reducing hemodynamic changes, or potentiating the analgesic effect.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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