General Anesthetic Management of a Patient With Hypertrophic Cardiomyopathy for Oral Surgery: Did Digitalis Contribute to Bradycardia?

Aiji Sato(Boku), DDS, PhD,* Maki Morita, DDS,† MinHye So, MD,‡ Tetsuya Tamura, MD, PhD,‡ Fumiaki Sano, MD,‡ Yasuyuki Shibuya DDS, PhD,§ Jun Harada, MD, PhD,|| and Kazuya Sobue, MD, PhD¶

*Associate Professor, Department of Anesthesiology, Aichi Gakuin University School of Dentistry, Nagoya, Japan; †Resident, Department of Oral and Maxillofacial Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; ‡Assistant Professor, Department of Anesthesiology and Intensive Care Medicine, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; §Professor, Department of Oral and Maxillofacial Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; ||Professor, Department of Anesthesiology, Aichi Gakuin University School of Dentistry, Nagoya, Japan; and ¶Professor, Department of Anesthesiology and Intensive Care Medicine, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

Stabilization of circulatory dynamics is a critical issue in the anesthetic management of patients with hypertrophic cardiomyopathy (HCM). In this report, we managed general anesthesia for a 74-year-old male patient with nonobstructive HCM who developed circulatory instability intraoperatively. Severe bradycardia measuring 35 beats/min and hypotension measuring 78 mm Hg systolic were observed during surgery. Using stroke volume variation and stroke volume from the FloTrac as indices, successful circulatory management was performed with dopamine. The hypotension and bradycardia were thought to be the result of methyldigoxin and possibly associated with our perioperative management. Cardiology consult should have been obtained. We demonstrated that the FloTrac can be beneficial in diagnosing and managing cardiovascular instability and administration of dopamine in the anesthetic management of nonobstructive HCM patients.

Key Words: Hypertrophic cardiomyopathy; Circulation management; Digitalis; Dopamine; FloTrac.

Apical hypertrophic cardiomyopathy (AHCM) is found in up to 25% of Japanese patients diagnosed with hypertrophic cardiomyopathy (HCM).¹ Although most patients with AHCM experience minimal to no symptoms, a variety of signs and symptoms can occur, including atrial fibrillation, ventricular tachycardia, and angina.² Electrocardiographic findings can include T-wave inversion, particularly in the left precordial leads. A spade-like configuration of the left ventricular cavity at the end of diastole on left ventriculography is the typical feature of AHCM.^{3,4} Patients with AHCM can present with serious cardiac complications, such as

progressive heart failure, myocardial infarction, and sudden cardiac death, although AHCM is generally associated with a better prognosis than other forms of HCM.^{2,5} Generally speaking, pathophysiological characteristics of HCM associated with cardiac hypertrophy are stenosis and obstruction of the left ventricular outflow tract (LVOT), ventricular diastolic dysfunction, myocardial ischemia, and arrhythmia. In both hypertrophic obstructive cardiomyopathy and nonobstructive HCM, the thickened left ventricle reduces ventricular size, with resultant stiffness reducing left ventricular end-diastolic volume.

Particularly in hypertrophic obstructive cardiomyopathy, decreased preload and afterload and increased myocardial contractility can worsen LVOT obstruction and cause decreased cardiac output.⁶ Therefore, stabilization of circulatory dynamics is critical in anesthetic management. In this report, we describe compromised circulatory management during general anesthesia in a patient with nonobstructive HCM taking digitalis.

Received November 1, 2017; accepted for publication January 9, 2018.

Address correspondence to Dr Aiji Sato(Boku), Department of Anesthesiology, Aichi Gakuin University School of Dentistry, 2-11 Suemori-dori, Chikusaku, Nagoya 464-8651, Japan; bokuaiji@dpc.aichi-gakuin.ac.jp.

Anesth Prog 65:192–196 2018 | DOI 10.2344/anpr-65-03-12
© 2018 by the American Dental Society of Anesthesiology

Table 1. Medical History Timeline*

Date	Event
1985	Diagnosed with HCM (no medication)
2016	Increased pain and tenderness of the right mandible; diagnosed with mandibular osteomyelitis
Jan 2017	Digitalis was prescribed for HCM by patient's local physician
Apr 2017	Surgery for mandibular osteomyelitis was performed under general anesthesia

* HCM indicates hypertrophic cardiomyopathy.

Written consent for this publication has been obtained from the patient.

CASE REPORT

The patient was a 74-year-old male whose height was 159 cm and whose weight was 57 kg (body mass index = 22.5). He had been diagnosed with HCM at age 42 but no treatment was provided due to lack of symptoms associated with cardiac insufficiency, including syncope, chest pain, and palpitations. In January 2017, methyl-digoxin (0.2 mg/d) and dipyridamole (75 mg/d) were prescribed by his local physician, although the reason is unclear (Table 1). He had been referred to the Nagoya

City University Graduate School of Medical Sciences Department of Oral and Maxillofacial Surgery for evaluation of right mandibular tenderness diagnosed as osteomyelitis. Preoperative evaluation revealed moderate cardiac enlargement by chest radiograph (cardiothoracic ratio: 52%).

Sinus bradycardia (heart rate: 44 beats/min) and negative T waves (II, III, aV_F, V3–6) were observed by 12-lead electrocardiogram (Figure). Echocardiography revealed that left ventricular wall motion was within the normal range, with a left ventricular ejection fraction of 63%. Systolic anterior motion of the mitral valve was not observed; however, moderate aortic regurgitation and mild mitral regurgitation were observed. Cardiac enlargement around the entire left ventricular apex was observed, and therefore the patient was diagnosed with AHCM. Complete blood cell counts, serum chemistry, and blood coagulation studies revealed no abnormalities. Curettage was planned to treat right mandibular osteomyelitis under general anesthesia, which was 3 months after the methyl-digoxin and dipyridamole had been prescribed.

Our anesthetic goals included:

1. Avoiding factors that worsen LVOT obstruction, such as tachycardia, dehydration, and peripheral vasodilators.

Preoperative 12-lead electrocardiogram. Sinus bradycardia (heart rate 44 beats/min) and negative T wave (II, III, aV_F, V3–6) were observed.

Table 2. Vital Signs and Cardiovascular Values*

	<i>Before Induction of Anesthesia</i>	<i>During Crisis, Value (% Down)</i>	<i>After Dopamine Infusion</i>
HR, beats/min	48	35 (27)	50
SBP, mm Hg	130	78 (40)	100
CI, L/min/m ²	2.5	1.5 (40)	3
SV, mL/beat	70	30 (58)	60
SVV, %	9	5 (45)	9

* HR indicates heart rate; SBP, systolic blood pressure; CI, cardiac index; SV, stroke volume; and SVV, stroke volume variation.

2. Maintaining appropriate preload and afterload.
3. Having adequate intraoperative and postoperative pain control.

For the anesthesia procedure, the patient fasted from solids for greater than 8 hours and had 300 mL clear fluids thereafter with nothing per os for 2 hours prior to the procedure. This was the first case of the day, to minimize dehydration. Blood pressure and heart rate before induction of anesthesia were 130/65 mm Hg and 48 beats/min, respectively. In addition to standard monitoring (including pulse oximetry, 5-lead electrocardiogram, capnography, and noninvasive arterial blood pressure), arterial blood pressure monitoring was planned after induction with FloTrac placed to estimate preload and afterload. Baseline vital signs in the operating room are noted in Table 2. An intravenous line was inserted in the left forearm and anesthesia was induced by 3 mcg/mL propofol (target-controlled infusion), 100 µg fentanyl, and 0.2 mcg/kg/min remifentanyl. Then, 40 mg of rocuronium was administered for muscle relaxation, followed by nasotracheal intubation. An arterial line in the left radial artery for direct measurement of arterial pressure was then placed. Cardiac output, stroke volume (SV), stroke volume variation (SVV), and cardiac index (CI), which function as reference indices for preload/afterload, were continuously monitored by a Vigileo monitor using FloTrac (Edward Lifesciences Co, Tokyo, Japan.). The SVV, CI, and SV after the induction of anesthesia were 9%, 2.5 L/min/m², and 70 mL/beat, respectively (normal ranges: SVV 10~15%, CI 2.5~4 L/min/m², SV 60~100 mL/beat). Anesthesia was maintained by continuous infusion of propofol at 2–3 mcg/mL (target-controlled infusion) and remifentanyl at 0.15 mcg/kg/min with 40% oxygen and 60% air. Severe bradycardia measuring 35 beats/min and hypotension of 78 mm Hg systolic were observed 45 minutes after induction during surgery. Atropine sulfate 0.5 mg was administered twice (total dose of 1 mg), but it had no effect. In order to maintain adequate amnesia, we maintained continuous

infusion of propofol at 2 mcg/mL (target-controlled infusion). The SVV during this time was 5%, with CI of 1.5 L/min/m² and SV of 30 mL/beat. We were concerned with administering phenylephrine due to possible reflex bradycardia, as vagal nerve blockade with atropine was ineffective. Circulatory management was therefore provided with dopamine started and maintained at 3 mcg/kg/min. This improved the patient's heart rate to 50 beats/min, blood pressure to 100 mm Hg systolic, SVV 9%, CI to 3.0 L/min/m², and SV to 60 mL/beat within 10 minutes of administration (Table 2). Before the end of the surgery, we administered 1000 mg acetaminophen to provide postoperative pain control. No local anesthesia was administered for surgery or postoperative pain control. After surgery, 100 mg of sugammadex was administered after neuromuscular monitoring before extubation. We confirmed response to eye-opening command, sufficient spontaneous respiration, and stable hemodynamics prior to extubation. The surgery time was 1 hour and 31 minutes, and anesthesia time was 2 hours and 45 minutes. The patient was monitored in the postanesthesia care unit for 1 hour before transfer to the general ward of our dental hospital after confirming he met discharge criteria.

DISCUSSION

In the anesthetic management of patients with HCM, particularly with LVOT obstruction, increased myocardial contractility, decreased preload and afterload, and tachycardia can enhance outflow tract obstruction. Therefore, the pressure gradient in the LVOT needs to be well optimized.⁷ As LVOT obstruction presents as heart failure and can place a patient at risk of sudden death, achieving stable hemodynamics is critical. The hypotension and bradycardia in our patient were thought to be the result of methyldigoxin, possibly associated with our perioperative management. Digoxin is indicated for congestive heart failure, valvular disease, tachycardia arising from atrial fibrillation and flutter, and paroxysmal tachycardia. The positive inotropic effect of digoxin is associated with an increase in intracellular calcium ions leading to increased myocardial contractility. The negative chronotropic effect is also due to an increase in intracellular calcium, which lengthens phase 0 and phase 4, leading to a delay of the conduction velocity and prolongation of the refractory period. In addition, vagal stimulation of the atrioventricular node causes a decrease in heart rate. There are published recommendations to continue digoxin therapy before surgery.^{8,9} Digoxin continues to be useful for patients with congestive heart failure and left ventricular

dysfunction who remain symptomatic despite receiving ACE inhibitors, beta adrenergic blockers, and diuretics. Digoxin is the only positive inotropic drug that does not increase mortality in congestive heart failure.⁹ If digoxin is stopped perioperatively, heart rate control and positive inotropy should be maintained with other drugs.¹⁰ Digoxin and its derivatives, however, are relatively contraindicated in patient with hypertrophic obstructive cardiomyopathy because digoxin increases cardiac inotropy. Its negative chronotropic effect would otherwise be beneficial. Other medications for the treatment of HCM include calcium antagonists,^{11,12} beta blockers,^{13,14} and sodium channel blockers.^{15,16} Although our patient was prescribed digoxin by his local family physician, presumably to prevent heart failure or to reduce heart rate, it would have been prudent to send this patient to a cardiologist for consultation regarding the appropriateness of methyl digoxin and possible replacement with a beta blocker or other medication.

Our perioperative management may also have contributed to this patient's hemodynamic instability. We chose a predominantly opioid-based anesthetic with remifentanyl. Propofol, used for amnesia and hypnosis, is a potent vasodilator, which may have contributed to afterload reduction. It is possible that our patient may have been relatively hypovolemic, and judicious intravenous fluid loading might have been beneficial to mitigate the effects of propofol vasodilation. There was, however, no significant hypotension or bradycardia immediately following induction.

We evaluated left ventricular preload and cardiac output in our patient using FloTrac. The FloTrac system is composed of the FloTrac sensor and Vigileo monitor. The FloTrac system uses arterial pressure-based cardiac output, which is based on the relationship between pulse pressure and SV. This principle, as well as recent advances in signal processing, has led to the development of this system that can continuously measure cardiac output from an arterial pressure waveform that does not require an external calibration reference method.¹⁷

The FloTrac measures hemodynamic parameters including SV, SVV, and SVR. SV and SVV are important indices of left ventricular preload, and SVV in particular serves as an index of infusion reactivity during ventilatory support. Fluid management may be guided by FloTrac, as Peel et al¹⁷ recommend a SVV of 10% to 15% as an index of infusion load. There are a number of published papers that describe the efficacy of FloTrac,^{7,18–22} although its reliability has also been questioned by others.^{23–25} It may be particularly helpful as a trend monitor for an individual patient, as in our case presentation.

A previous report has suggested the usefulness of FloTrac in the anesthetic management of HCM patients.⁷ During episodes of significant bradycardia and hypotension, SV and SVV can be extremely important indices for determining management. During our patient's hypotensive episode, the SVV was 5% and SV was 30 mL/beat. Thus, rather than boosting blood pressure with an infusion load, we felt it was appropriate to promptly use an inotrope. The patient's bradycardia did not improve even with the use of atropine, and, out of fear for further bradycardia, we were concerned with the use of phenylephrine due to reflex bradycardia and possibly decreased SV. We therefore performed hemodynamic management using low-dose dopamine, whereupon the patient's bradycardia of 35 beats/min improved to 50 beats/min and blood pressure improved from 78 to 100 mm Hg systolic. Other cardiac indices normalized based on FloTrac approximating preinduction values. Due to the risk of exacerbating LVOT obstruction in the anesthetic management of HCM, drugs with positive inotropic effects, such as catecholamines, can be difficult to use as a treatment for deteriorating hemodynamics.⁷ Our patient did not significant have signs of outflow obstruction, and we chose dopamine as it can be carefully titrated for both alpha and beta effects. In this way, we felt we could obtain better rate control without excessive tachycardia or inotropy. Higher heart rate with the use of dopamine may also have been avoided due to the bradycardic effect of methyl digoxin. Another option could have been to administer noradrenaline to maintain afterload and to boost blood pressure. The reflex bradycardia from noradrenaline is usually offset by its mild positive chronotropic effects, resulting in minimal changes in heart rate. In our patient, we felt the bradycardia needed to be treated as well as the blood pressure, and hence dopamine was selected.

In conclusion, we managed general anesthesia for a patient with AHCM who developed hemodynamic instability managed with dopamine. We demonstrated that FloTrac can be useful in diagnosing and managing circulatory instability. The hypotension and bradycardia in this patient may have been partly the result of methyl digoxin. Preoperative consultation with cardiology would likely have been beneficial to confirm appropriate medication management for this patient's cardiomyopathy. This suggests the need for comprehensive preanesthetic workup in such cases.

REFERENCES

1. Karan K, Amal C, Matthew CE, Amish S. Apical hypertrophic cardiomyopathy among non-Asians: a case series and review of the literature. *Cardiol Res.* 2016;7:46–50.

2. Maron MS, Finley JJ, Bos JM, et al. Prevalence, clinical significance, and natural history of left ventricular apical aneurysms in hypertrophic cardiomyopathy. *Circulation*. 2008; 118:1541–1549.
3. Sakamoto T, Tei C, Murayama M, Ichiyasu H, Hada Y. Giant t wave inversion as a manifestation of asymmetrical apical hypertrophy (AAH) of the left ventricle. Echocardiographic and ultrasono-cardiotomographic study. *Jpn Heart J*. 1976;17:611–629.
4. Yamaguchi H, Ishimura T, Nishiyama S, et al. Hypertrophic nonobstructive cardiomyopathy with giant negative T waves (apical hypertrophy): ventriculographic and echocardiographic features in 30 patients. *Am J Cardiol*. 1979; 44:401–412.
5. Eriksson MJ, Sonnenberg B, Woo A, et al. Long-term outcome in patients with apical hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2002;39:638–645.
6. Reich DL, Brooks JL, Kaplan JA. Uncommon cardiac diseases. In: Kats J, Benumof JL, Dabis LB, eds. *Anesthesia and Uncommon Diseases*. Philadelphia, PA: WB Saunders; 1990:341.
7. Shinohara T, Taga N, Kadosaki M, Wainai T, Kaneko A, Takeuchi M. Anesthetic and circulatory management of pancreatic and adrenal tumor surgery in a patient with hypertrophic obstructive cardiomyopathy (HOCM) using FloTrac monitoring system. *Circ Control*. 2011;32:181–184.
8. Nagelhout J, Elisha S, Waters E. Should I continue or discontinue that medication? *AANA J Course*. 2009;77:59–73.
9. Groban L, Butterworth J. Perioperative management of chronic heart failure. *Anesth Analg*. 2006;103:557–575.
10. Alwyn K, Simon JH. Heart failure: pathophysiology, risk assessment, community management and anaesthesia. *Contin Educ J Anaesth Crit Care Pain*. 2008;8:161–166.
11. Maron BJ. Hypertrophic cardiomyopathy. *Curr Probl Cardiol*. 1993;18:639–704.
12. Nagano M, Omote S, Takizawa A, Yasue H. Effect of diltiazem on left ventricular isovolumic relaxation time in patients with hypertrophic cardiomyopathy. *Jpn Circ J*. 1983; 47:54–58.
13. DeRose JJ, Babas JS, Winters SL. Current on sudden cardiac death in hypertrophic cardiomyopathy. *Prog Cardiovasc Dis*. 1994;36:475–484.
14. Doiuchi J, Hamada M, Ito T, Kokubu T. Comparative effects of calcium-channel blockers and beta adrenergic blocker on early diastolic time intervals and a-wave ratio in patients with hypertrophic cardiomyopathy. *Clin Cardiol*. 1987; 10:26–30.
15. Pollick C. Muscular subaortic stenosis: hemodynamic and clinical improvement after disopyramide. *N Engl J Med*. 1982;307:907–999.
16. Pollick C. Disopyramide in hypertrophic cardiomyopathy. II. Noninvasive assessment after oral administration. *Am J Cardiol*. 1988;62:1252–1255.
17. Peel A, Pizow R, Cotev S. Systolic blood pressure variation is a sensitive indicator of hypovolemia in ventilated dogs subjected to graded hemorrhage. *Anesthesiology*. 1987;67: 498–502.
18. Isao F. Clinical usefulness of the Flo Trac system—efficacy of arterial pressure-based cardiac output and stroke volume variations. *J Jpn Soc Clin Anesth*. 2011;31:81–90.
19. Yoshifumi K. Circulatory, fluid management and patient outcome. *J Jpn Soc Clin Anesth*. 2011;30:398–409.
20. Kenji I, Toshiyasu S. Efficacy and future of new monitoring parameters. *J Clin Anesth (Jpn)*. 2009;33:535–541.
21. Shunsuke S, Sumie E, Yuuichiro K, Matsuhisa S, Takero A, Yasuhisa O. Intraoperative fluids management using stroke volume variation as an indicator radical prostatectomy. *J Clin Anesth (Jpn)*. 2009;36:1179–1182.
22. Kohei F, Yasuo T, Tomohiro S, Michiko K, Katsuya T, Shuzo O. Emergency anesthesia in a patient with von Hippel-Lindau syndrome who underwent pheochromocytectomy and the resection of cerebellar hemangioblastoma. *J Jpn Soc Clin Anesth*. 2011;31:884–887.
23. Comton FD, Zukunft B, Hoffman C, Zidek W, Schaefer JH. Performance of a minimally invasive uncalibrated cardiac output monitoring system (FloTrac/Vigileo) in haemodynamically unstable patients. *Br J Anaesth*. 2008;100:451–456.
24. Lørsomradee S, Cromheecke S, De Hert SG. Uncalibrated arterial pulse contour analysis versus continuous thermodilution technique: effect of alterations in arterial waveform. *J Cardiothorac Vasc Anesth*. 2007;21:636–643.
25. Opdam HI, Wan L, Bellomo R. A pilot assessment of the FloTrac cardiac output monitoring system. *Intensive Care Med*. 2007;33:344–349.