



Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Case Report

Role of Rescue Transesophageal Echocardiography During Intraoperative Anaphylaxis Complicated by Dynamic Left Ventricular Outflow Tract Obstruction

Nishank P. Nooli, MD^{*,1}, Matthew A. Jensen, MD[†],
 Prentiss Lawson Jr., MD[†], Benjamin C. Tuck, MD^{*},
 Sandra S. Sipe, MD[‡], Navin C. Nanda, MD[‡],
 Matthew Townsley, MD[§]

^{*}Division of Cardiothoracic Anesthesia, Department of Anesthesiology and Perioperative Medicine, University of Alabama at Birmingham, Birmingham, AL

[†]Department of Anesthesiology and Perioperative Medicine, University of Alabama at Birmingham, Birmingham, AL

[‡]Division of Cardiovascular disease, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL

[§]Division of Pediatric Cardiac Anesthesia, Department of Anesthesiology and Perioperative Medicine, University of Alabama at Birmingham, Birmingham, AL

Key Words: anaphylaxis; serum tryptase; left ventricle; two-dimensional transesophageal echocardiogram; left ventricle outflow tract; systolic anterior motion

ANAPHYLAXIS IS SUSPECTED when there is dysfunction in ≥ 2 organ systems after exposure to a suspected antigen.¹ Findings may include urticaria, mucosal edema, gastrointestinal distress, bronchospasm, or hypotension. It also can be diagnosed in adults who have a sudden decrease in systolic blood pressure to <90 mmHg or a $\geq 30\%$ decrease from baseline blood pressure after exposure to a known allergen. An elevated serum tryptase concentration helps to confirm the diagnosis, as it is a marker for mast cell degranulation.² However, in patients with end-stage renal disease (ESRD), tryptase has been shown to be elevated at baseline, which confounds the diagnosis of anaphylaxis.³ In the perioperative setting, there are numerous possible triggers for allergic reactions and anaphylaxis, including neuromuscular blocking agents,

antibiotics, blood products, chlorhexidine, and latex.⁴ The first-line treatment for anaphylaxis is epinephrine, a proven life-saving intervention.⁵ Herein, the authors describe the usefulness and importance of 2-dimensional echocardiography in altering the management of an adult patient undergoing renal transplant surgery experiencing anaphylaxis resulting from antibiotic administration. Echocardiography revealed significant left ventricular outflow tract (LVOT) obstruction as the etiology of worsening hemodynamic collapse refractory to epinephrine administration. This finding prompted the institution of appropriate measures to treat concomitant anaphylaxis and dynamic LVOT obstruction, resulting in full patient recovery.

Case Report

A 56-year-old African American female patient with a history of ESRD secondary to membranous nephropathy presented to the operating room for a deceased donor renal transplant. The patient consented to have the following case details and images published in this report. Her past medical

Abbreviation: bpm, beats per minute

¹Address correspondence to Nishank P. Nooli, MD, Assistant Professor, Division of Cardiothoracic Anesthesia, Department of Anesthesiology and Perioperative Medicine, University of Alabama at Birmingham, 619 19th Street South, JT 845, Birmingham, AL 35249-6810.

E-mail address: nnooli@uabmc.edu (N.P. Nooli).

<https://doi.org/10.1053/j.jvca.2022.12.014>

1053-0770/© 2022 Elsevier Inc. All rights reserved.

history was significant for sickle cell trait, hypertension, and allergies to doxycycline and sulfa drugs. During her initial transplant evaluation, a preoperative transthoracic echocardiogram (TTE) showed normal left ventricular (LV) function with concentric remodeling and proximal septal thickening (13 mm) with a narrow LVOT but no evidence of obstruction. The peak LVOT velocity was 85.3 cm/s. The remainder of her transplant evaluation was unremarkable.

In the operating room, general anesthesia was induced with lidocaine, propofol, fentanyl, and rocuronium. She was hemodynamically stable during induction. A noncoated central venous line was placed using chlorhexidine for skin sterilization. Approximately 30 minutes later, the patient received cefazolin. Shortly thereafter, she became hypotensive (blood pressure decreased to 60/24 mmHg from a baseline of 110–120/60 mmHg), tachycardic (heart rate increased to 110–120 bpm from a baseline of 70–75 bpm), and had decreased end-tidal carbon dioxide levels. She remained in a normal sinus rhythm. There were no cutaneous findings (ie, urticaria), and peak airway pressures were slightly increased from 14–to–18 cmH₂O. Anaphylaxis was high on the differential diagnosis due to the abrupt onset of profound hypotension, with other possible causes including cardiac tamponade, pulmonary embolism, anesthetic-induced vasodilation, tension pneumothorax, and myocardial ischemia. Multiple boluses of dilute epinephrine (10 µg/mL) were administered immediately, along with aggressive fluid resuscitation and administration of adjunct medications, including diphenhydramine and dexamethasone. However, there was no response to these therapies and the patient's hemodynamic status continued to worsen. For further assessment, a 2-dimensional transesophageal echocardiogram (TEE) was performed by a cardiac anesthesiologist using a commercially available EPIQ 7 ultrasound system (Philips Healthcare, Andover, MA) and an X7-2t transducer. A hyperdynamic LV with significant systolic anterior motion (SAM) of the anterior mitral leaflet causing dynamic LVOT obstruction was noted (Fig 1; Videos 1 and 2). Continuous-wave spectral Doppler tracing showed a peak LVOT gradient

of 57 mmHg (Fig 2). The TEE examination demonstrated no regional wall motion abnormalities, additional valvular pathology, pericardial effusion, or right ventricular pathology (including dilatation or hypokinesis or abnormal septal motion suggestive of pulmonary embolism). Although epinephrine is considered the first-line treatment for anaphylaxis, given its positive chronotropic and dromotropic effects, its use exacerbated the patient's dynamic LVOT obstruction. Therefore, epinephrine was held while aggressive fluid administration was continued, along with the addition of phenylephrine and vasopressin boluses, which improved her hemodynamics. The administration of both fluid and vasopressor boluses was titrated carefully to ensure adequate LV filling and resolution of LVOT obstruction, visualized in real-time with TEE monitoring. It was critical to eventually resume a low-dose epinephrine infusion for the treatment of anaphylaxis, along with continued fluid administration and vasopressor support. Transesophageal echocardiogram guidance played a vital monitoring role in ensuring no further dynamic LVOT obstruction occurred during this time.

Additionally, the patient's serum tryptase fluorescent enzyme immunoassay was elevated at 21.8 ng/mL (N <11.0 ng/mL). Her surgery was postponed, and she was transported to the intensive care unit for further monitoring and treatment. After hemodynamic stabilization, she underwent an uneventful renal transplant later that day.

Discussion

Perioperative Anaphylaxis

Perioperative anaphylaxis occurs in approximately 1:3,500–to–1:20,000 anesthetics and is commonly due to exposure to neuromuscular blocking agents, antibiotics, blood products, chlorhexidine, or latex.⁶ As opposed to a nonintubated patient who can report symptoms (eg, shortness of breath, tongue or throat swelling, itching), in the perioperative setting, the diagnosis is often delayed, as cardiovascular

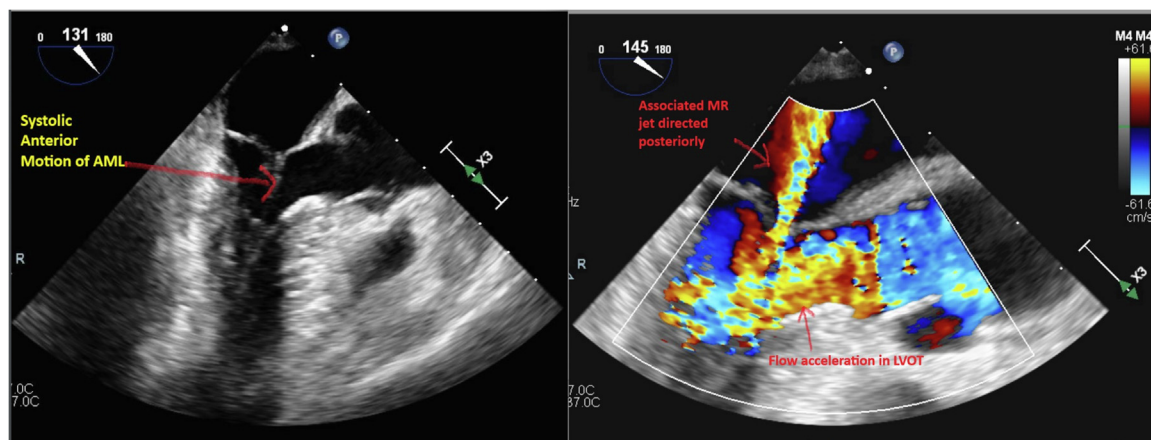


Fig 1. Midesophageal long-axis transesophageal echocardiogram view on the left side showing systolic anterior motion of the anterior mitral leaflet and the zoomed-in view on the right with color-flow Doppler showing flow acceleration in the left ventricular outflow tract with an associated mitral regurgitation jet directed posteriorly, consistent with dynamic left ventricular outflow tract obstruction secondary to systolic anterior motion. AML, anterior mitral leaflet; LVOT, left ventricular outflow tract; MR, mitral regurgitation.

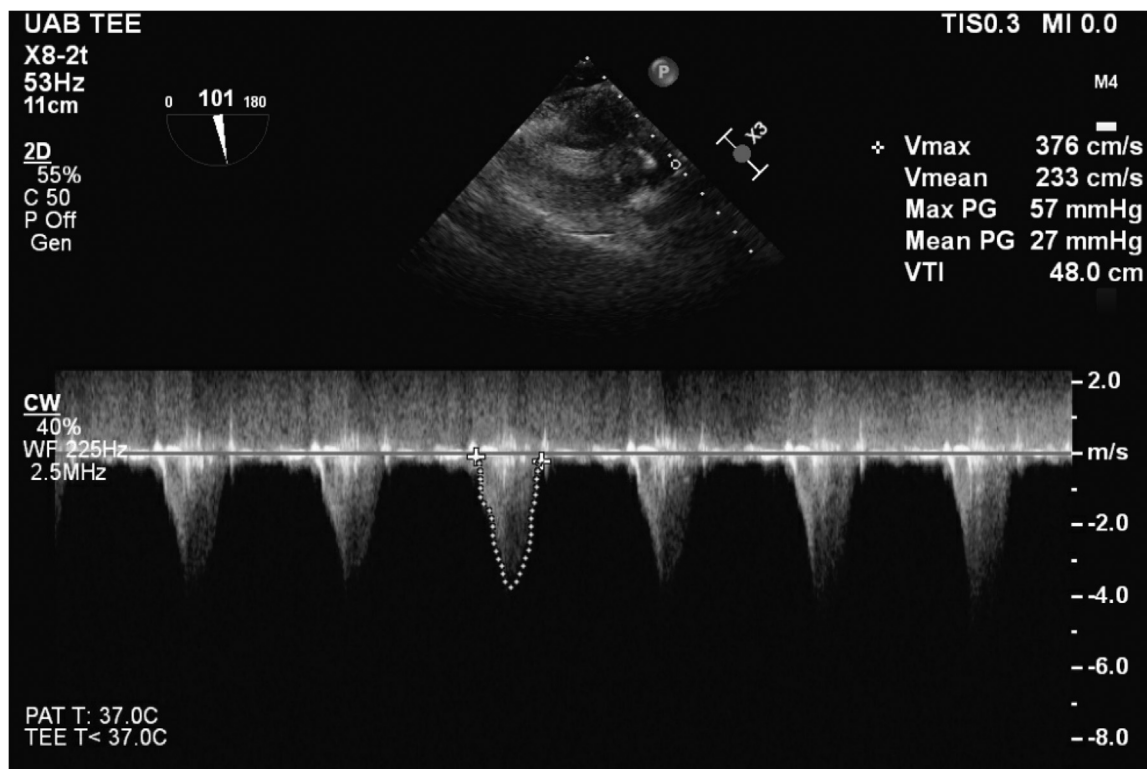


Fig 2. Continuous-wave spectral Doppler tracing through the aortic valve in transgastric long-axis view on transesophageal echocardiography shows a late peaking waveform with a peak gradient of 57 mmHg, consistent with dynamic left ventricular outflow tract obstruction. TEE, transesophageal echocardiography.

collapse is typically the only presenting sign of anaphylaxis.^{2,6} Treatment begins with prompt recognition followed by administration of epinephrine, which was done in this patient. Delaying epinephrine administration in the setting of anaphylaxis is associated with poor outcomes.⁷ World Allergy Organization guidelines, as well as those from various other countries, agree upon the use of epinephrine as first-line therapy for anaphylaxis, but there is some disparity regarding the use of second-line adjuvant therapies, including the debatable use of steroids.⁸ Although with low certainty of evidence, recent guidelines advise against the routine use of steroids in anaphylaxis. Steroid administration is only recommended to treat underlying asthma or in cases of epinephrine refractory shock. Antihistamines are recommended to treat dermatologic symptoms but have no role in treating respiratory or cardiovascular symptoms of anaphylaxis.^{9,10} Glucagon may be used in patients with a suboptimal response to epinephrine. Particularly, this includes patients on β -blockers.¹⁰

There were numerous potential causes of anaphylaxis in this patient. She received rocuronium during the induction of anesthesia to facilitate tracheal intubation, chlorhexidine during central line insertion, and a latex Foley catheter after induction. During the initial stabilization of the patient, the latex Foley catheter was removed and replaced with a latex-free catheter. Finally, she received cefazolin as a prophylactic antibiotic. She was hemodynamically stable until the point when she received the antibiotic; therefore, her reaction was thought to be due to the cefazolin administration, one of the most

common culprits of anaphylaxis.⁶ The timing of the onset of symptoms in relation to the exposure occasionally can be helpful in determining the inciting agent. Retrospectively, in reviewing the patient's previous anesthetic records, it was noted that she had received cefazolin for surgical prophylaxis 8 years prior to this current encounter with no issues. Neuromuscular blocking agents, antibiotics, and hypnotics generally show symptoms of anaphylaxis within 30 minutes of exposure; whereas chlorhexidine, latex, and blood products can take >30 minutes to cause a reaction.⁶ In this patient, during her renal transplant that occurred later in the day after stabilization, her skin was again prepped with chlorhexidine; however, the latex-free Foley catheter was left in place. A different antibiotic was chosen for prophylaxis, and she did not have any further allergic reactions.

Tryptase in Patients With ESRD

Tryptase is a mast cell-specific protease that is secreted at rest in a protryptase form. Additional pro-tryptase molecules are stored inside mast cell granules, converted to mature tryptase, and secreted upon mast cell activation. The total tryptase level (both pro- and mature forms) can be measured to confirm clinical suspicion of mast cell degranulation during a hypersensitivity reaction.¹¹ A 2012 consensus paper suggested that mast cell activation should be suspected when the acute serum total tryptase is >20% plus 2 ng/mL over the baseline level.¹² In a 2019 French study, when compared to 3 other algorithms

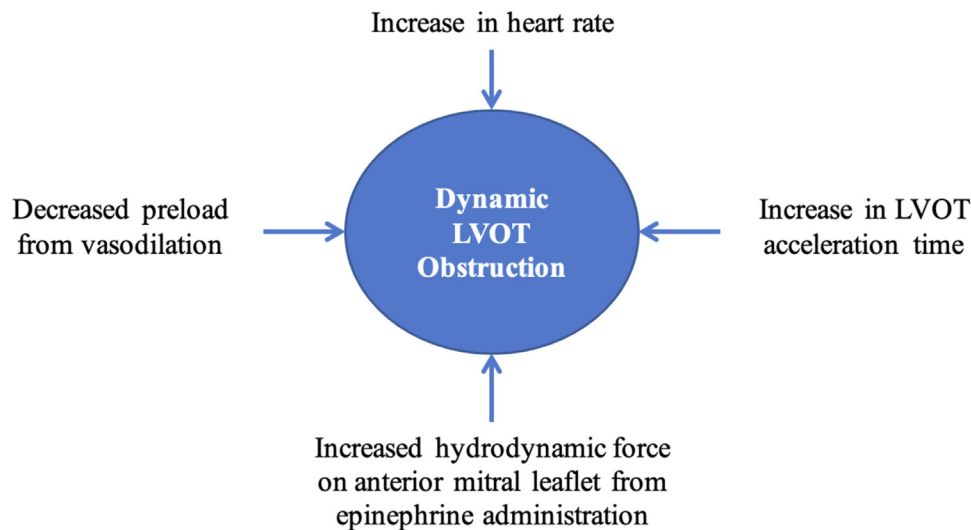


Fig 3. Summary of the factors that resulted in a dynamic left ventricular outflow tract obstruction. LVOT, left ventricular outflow tract.

used to diagnose perioperative anaphylaxis, this definition was again shown to be the most accurate.¹¹ Unfortunately, the authors' patient herein did not have a baseline serum tryptase level measured after the resolution of symptoms for comparison.

Serum tryptase levels have been shown to increase with worsening renal function.³ Patients with an estimated glomerular filtration rate of <15 mL/min (but not on hemodialysis), as was the case with this patient, had a baseline serum tryptase level of 13.76 ± 7.79 ng/mL.³ Her elevated tryptase level of 21.8 ng/mL was slightly higher than one SD above what would be expected based on her pretransplant kidney function. However, a limitation was that her serum tryptase was measured approximately 2.5 hours after the suspected anaphylactic event, which is outside of the recommended time frame of 0.5–to–1.5 hours cited in previous studies when the tryptase levels peak.¹¹ Had the serum tryptase level been drawn closer to the inciting event, it is possible that it would have been more elevated.

Dynamic LVOT Obstruction

In the setting of suspected anaphylaxis, hypotension refractory to epinephrine should raise suspicion for other pathologies and requires further investigation. By itself, general anesthesia can predispose patients to SAM of the anterior mitral leaflet due to the vasodilatory effect of volatile anesthetics and intravenous induction agents. Patients are often slightly hypovolemic from their *nil per os* status prior to surgery. The combination of hypovolemia and vasodilation causing decreased preload results in an underfilled LV that can change the geometry of the ventricle, moving the papillary muscles relatively anterior.⁷ In this patient, the decreased preload due to vasodilation as the result of inflammatory mediators and general anesthesia, coupled with the physiologic changes seen with epinephrine administration (ie, an increase in heart rate, reduced diastolic filling time, increase in LVOT acceleration time, increase in hydrodynamic force on the anterior mitral

leaflet), resulted in LV collapse and a dynamic LVOT obstruction that was found by TEE (Fig 3). Preoperative TTE findings of the hypertrophied proximal ventricular septum and a narrow LVOT made her more vulnerable to the development of SAM and LVOT obstruction from hypotension due to anaphylaxis and administration of an inotropic agent, such as epinephrine. Once this diagnosis was made, the patient was given intravenous fluids as well as boluses of phenylephrine and vasopressin to maintain blood pressure without causing any further increase in chronotropy or inotropy. The β -adrenoreceptor blockade also has been described to decrease the heart rate, increase diastolic filling time, and restore LV volume to relieve the dynamic LVOT obstruction,¹³ but was not useful in this hypotensive patient.

On review of the literature, a similar case of LVOT obstruction has been reported by Sadleir et al. regarding epinephrine-nonresponsive anaphylactic shock in an anesthetized patient.¹⁴ Interestingly enough, this patient also was undergoing renal transplantation. The use of echocardiography in both cases led to the inevitable discovery of the causative pathophysiology, which the authors would not have known otherwise. The authors' current report further serves to emphasize and increase awareness among anesthesiologists of the importance of performing TEE in an expedited manner when a patient becomes profoundly hypotensive during surgery due to suspected anaphylaxis and does not respond to epinephrine administration. There are also reports of intraoperative anaphylaxis leading to dynamic LVOT obstruction and cardiac arrest in patients with hypertrophic cardiomyopathy, in whom TEE played a vital role in diagnosis.^{15,16} On a different note, Wong et al., in their case of intraoperative anaphylaxis, described a finding of LV pseudohypertrophy¹⁷ noted on the TTE secondary to severe hypovolemia, which has been reported previously in association with cardiac tamponade.^{18,19} They used the term "pseudohypertrophy" as LV wall thickness was normalized after correction of hypovolemia when LV filling was optimized.

Summary

A sudden cardiopulmonary decline in the perioperative setting has a long list of differential diagnoses that must be considered. Anaphylaxis must be at the top of the list, as there are many potential inciting agents in the perioperative setting. Prompt treatment with epinephrine helps to stabilize mast cells, treat hypotension, and relieve bronchospasm. However, a worsening clinical picture despite appropriate treatment should suggest another underlying pathology, as was seen in the authors' patient in whom the inotropic and chronotropic effects of epinephrine led to dynamic LVOT obstruction. Laboratory confirmation of anaphylaxis with serum tryptase levels should always be considered, keeping in mind it could be elevated at baseline in patients with ESRD, confounding the diagnosis; whereas a baseline tryptase level 24 hours after resolution of symptoms would be helpful for comparison and confirmation. Although prompt administration of epinephrine is an essential treatment of anaphylaxis, this case highlighted the clinical conundrum that may occur when there is additional pathology (eg, dynamic LVOT obstruction) that is exacerbated by both the occurrence of anaphylaxis, as well as by the intervention to treat the anaphylaxis (ie, epinephrine). The authors believe echocardiography should be a part of the resuscitation algorithms in anaphylaxis patients who are not responsive to epinephrine therapy to quickly diagnose and manage additional life-threatening conditions.

Conflict of Interest

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1053/j.jvca.2022.12.014](https://doi.org/10.1053/j.jvca.2022.12.014).

References

- 1 Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: Summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006;117:391–7.
- 2 Sampson HA, Munoz-Furlong A, Bock SA, et al. Symposium on the definition and management of anaphylaxis: Summary report. *J Allergy Clin Immunol* 2005;115:584–91.
- 3 Sirvent AE, Gonzalez C, Enriquez R, et al. Serum tryptase levels and markers of renal dysfunction in a population with chronic kidney disease. *J Nephrol* 2010;23:282–90.
- 4 Garvey LH, Dewachter P, Hepner DL, et al. Management of suspected immediate perioperative allergic reactions: An international overview and consensus recommendations. *Br J Anaesth* 2019;123:e50–64.
- 5 Brown JC, Simons E, Rudders SA. Epinephrine in the management of anaphylaxis. *J Allergy Clin Immunol Pract* 2020;8:1186–95.
- 6 Volcheck GW, Hepner DL. Identification and management of perioperative anaphylaxis. *J Allergy Clin Immunol Pract* 2019;7:2134–42.
- 7 Fleming JT, Clark S, Camargo CA Jr., et al. Early treatment of food-induced anaphylaxis with epinephrine is associated with a lower risk of hospitalization. *J Allergy Clin Immunol Pract* 2015;3:57–62.
- 8 Alrasbi M, Sheikh A. Comparison of international guidelines for the emergency medical management of anaphylaxis. *Allergy* 2007;62:838–41.
- 9 Dodd A, Hughes A, Sargant N, et al. Evidence update for the treatment of anaphylaxis. *Resuscitation* 2021;163:86–96.
- 10 Cardona V, Ansotegui JJ, Ebisawa M, et al. [World Allergy Organization Anaphylaxis Guidance 2020]. *Arerugi* 2021;70:1211–34.
- 11 Vitte J, Amadei L, Gouitaa M, et al. Paired acute-baseline serum tryptase levels in perioperative anaphylaxis: An observational study. *Allergy* 2019;74:1157–65.
- 12 Valent P, Akin C, Arock M, et al. Definitions, criteria and global classification of mast cell disorders with special reference to mast cell activation syndromes: A consensus proposal. *Int Arch Allergy Immunol* 2012;157:215–25.
- 13 Ibrahim M, Rao C, Ashrafian H, et al. Modern management of systolic anterior motion of the mitral valve. *Eur J Cardiothorac Surg* 2012;41:1260–70.
- 14 Sadleir P, Clarke RC, Lim B, et al. Epinephrine (adrenaline) preventing recovery from intraoperative anaphylactic shock complicated by systolic anterior motion of the mitral valve with left ventricular outflow tract obstruction on transoesophageal echocardiography. *Anaesth Intensive Care* 2018;46:566–71.
- 15 Smith BB, Nickels AS, Sviggum HP. A rare combination of undiagnosed hypertrophic cardiomyopathy revealed by intraoperative anaphylaxis resulting in acute left ventricular outflow obstruction and cardiac arrest. *J Clin Anesth* 2016;31:212–4.
- 16 Yee KF, Wasowicz M. Anaphylaxis and cardiac surgery for hypertrophic obstructive cardiomyopathy: A case report and review of anaesthetic management. *Anaesthesiol Intensive Ther* 2016;48:252–6.
- 17 Wong CA, Arumugam S. Pseudohypertrophy of the left ventricle secondary to anaphylaxis: A case report. *Anaesth Intensive Care* 2019;47:295–9.
- 18 Di Segni E, Beker B, Arbel Y, et al. Left ventricular pseudohypertrophy in pericardial effusion as a sign of cardiac tamponade. *Am J Cardiol* 1990;66:508–11.
- 19 Feinberg MS, Popescu BA, Popescu AC, et al. Assessment of pseudohypertrophy as a measure of left-ventricular compression in patients with cardiac tamponade. *Cardiology* 2000;94:213–9.