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Anesthetic Management with Remimazolam in an Arrhythmogenic Right Ventricular Cardiomyopathy Patient with a History of Stable Sustained Ventricular Tachycardia: A Case Report

Hiroki Iwanaga [a], Hiroshi Aoki [a*], Yoshiaki Terao [a], Ekuko Fujimoto [a], Makito Oji [a], Natsuko Oji [a] and Tetsuya Hara [b]

[a] Department of Anesthesia, Nagasaki Rosai Hospital, 2-12-5 Setogoe, Sasebo 857-0134, Japan.
[b] Department of Anesthesiology and Intensive Care Medicine, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki, 852-8501 Japan.

Authors' contributions

This work was carried out in collaboration among all authors. Author HA experienced this case. Author HA wrote the first draft of the manuscript. Author YT supervised and reviewed this study. Authors YT, HI, EF, MO, NO and TH advised and revised the manuscript. All authors read and approved the final manuscript.

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Case Study

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**Corresponding author: E-mail: hiroshia@terra.dti.ne.jp;*

ABSTRACT

Aims: Arrhythmogenic right ventricular cardiomyopathy (ARVC) may cause sudden and unexpected deaths during the perioperative period. This study reports a case of ARVC, safely managed using total intravenous anesthesia with remimazolam.

Presentation of Case: A 51-year-old male patient (weight: 100.1 kg, height: 171.0 cm) with a history of ARVC underwent open cholecystectomy. The patient underwent total intravenous anesthesia with remimazolam, remifentanil, and a modified thoracoabdominal nerves block perichondrial approach for postoperative analgesia. Hemodynamic stability was maintained throughout the surgery. Catecholamine use was not warranted during the perioperative period. No episodes of stable sustained ventricular tachycardia or other cardiovascular episodes were observed.

Discussion and Conclusion: ARVC is a genetically-determined heart muscle disease characterized by life-threatening ventricular arrhythmias in apparently healthy young people. Anesthesiologists should pay close attention to the anesthetic management of patients with ARVC. Remimazolam can be safely used in such cases.

Keywords: Arrhythmogenic right ventricular cardiomyopathy; ventricular tachycardia; perioperative sudden cardiac death; electrocardiogram; β-blockers.

ABBREVIATIONS

ARVC : Arrhythmogenic Right Ventricular Cardiomyopathy
VT : Ventricular Tachycardia
PSCD : Perioperative Sudden Cardiac Death
ECG : Electrocardiogram
m-TAPA : Modified Thoracoabdominal Nerves Block Perichondrial Approach
NRS : Numerical Rating Scale

1. INTRODUCTION

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a rare but serious cardiovascular disease that can lead to heart failure, potentially fatal ventricular arrhythmias, and perioperative sudden cardiac death (PSCD) [1,2]. ARVC is an inherited heart disease with a prevalence of approximately 1:5,000 [3,4]. The average age of onset of ARVC is 30–40 years, and the disease is characterized by life-threatening ventricular arrhythmias in healthy young people [3,4]. The main goals of anesthesia in patients with ARVC are to maintain hemodynamic stability, minimize stress, and avoid tachycardia, hypertension, and hypotension [5]. Ventricular arrhythmias are exacerbated by β-adrenergic stimulation, whereas α-agonists are less likely to be arrhythmogenic [5]. PSCD can occur at any time during the perioperative period; therefore, sympathetic stimulation should be minimized by providing adequate analgesia [5]. Herein, we report a case of ARVC managed without ventricular arrhythmias using remimazolam.

2. PRESENTATION OF A CASE

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. Ethical approval for this study (Nagasaki Rosai No.05001, 2023/04/14) was provided by the Nagasaki Rosai Hospital Institutional Review Board, Sasebo, Japan.

A 51-year-old male patient (weight: 100.1 kg, height: 171.0 cm) with a history of ARVC was scheduled for open cholecystectomy.

The patient was presented to the emergency department with palpitations approximately 2 years before surgery. He had frequent episodes of ventricular tachycardia (VT). Electrocardiogram (ECG) showed stable sustained VT with positive QRS in II, III, and augmented vector foot and negative QRS in lead augmented vector left (Fig. 1). He was awake and alert, and his vital signs were unremarkable. This finding is consistent with a left bundle branch block in the inferior axis, as described in the 2010 ARVC Task Force Criteria (Table 1),

[6,7] which requires the presence of epsilon waves (red arrow) at V2 and V3, and inverted T waves at V1, V2, and V3 (Fig. 2). Echocardiography showed a right ventricular fractional area change of 22.43% (Fig. 3). The patient's family history of ARVC was unknown. The patient met the 2010 ARVC Task Force Criteria because three major criteria were met [6,7].

When the patient presented to the emergency department with a stable sustained VT, procainamide was administered. Afterward, amiodarone was administered due to the persistence of the stable sustained VT. Cardioversion was required due to the failure of medical therapy to manage his VT. He was then started on oral amiodarone and has not had VT since.

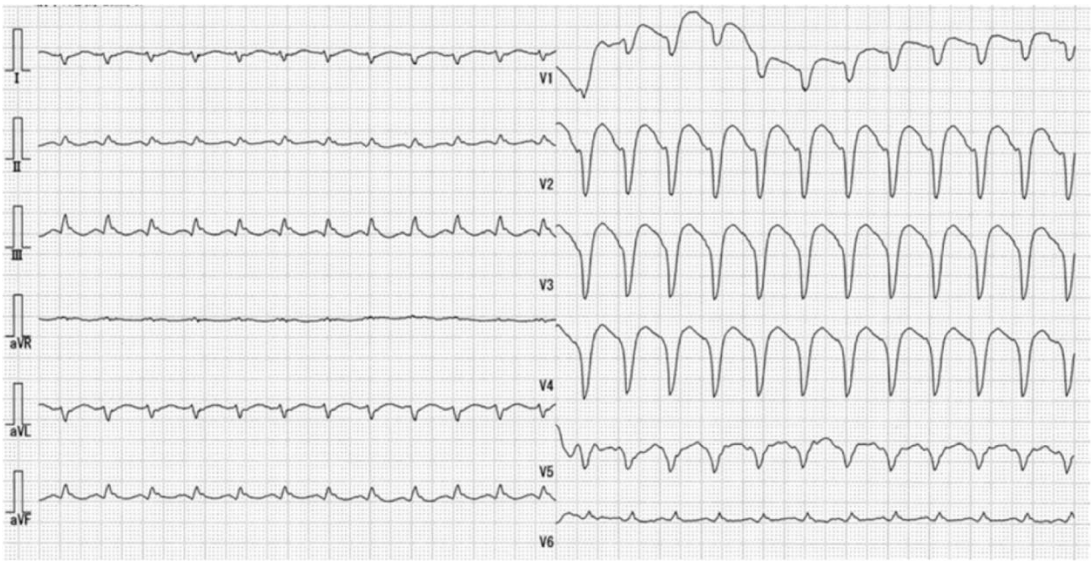

Fig. 1. Stable sustained ventricular tachycardia in the emergency department

The patient was presented to the emergency department with palpitations. An electrocardiogram (ECG) showed positive QRS complexes in leads II, III, and aVF and negative QRS complexes in lead aVL. These ECG findings are consistent with a left bundle branch block in the inferior axis, as described in the 2010 ARVC Task Force Criteria.

aVF, augmented vector foot; aVL, augmented vector left

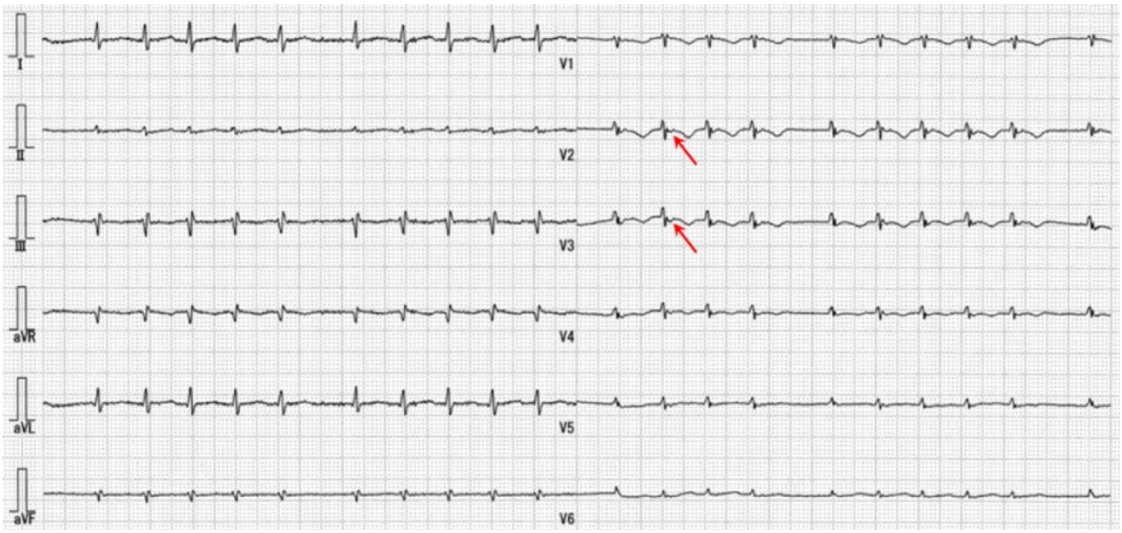

Fig. 2. Preoperative ECG

Epsilon waves (red arrows) are seen in leads V2 and V3 and inverted T waves in leads V1, V2, and V3. ECG, electrocardiogram

Table 1. 2010 revised task force criteria for the diagnosis of arrhythmogenic right ventricular cardiomyopathy [6,7]

Modified Task Force Criteria for ARVC – Diagnostic Categories Major and Minor Criteria		
Definite: two major or one major and two minor or four minor criteria from different categories Borderline: one major and one minor or three minor criteria from different categories Possible: one major or two minor criteria from different categories		
	Major	Minor
Global or regional dysfunction and structural alterations determined using echo, MRI, or RV angiography		
Echo	Regional RV akinesia, dyskinesia, or aneurysm and one of the following (end diastole): a) PLAX RVOT ≥ 32 mm (PLAX/BSA ≥ 19 mm/m^2) b) PSAX RVOT ≥ 36 mm (PSAX/BSA ≥ 21 mm/m^2) c) Fractional area change ≤ 33%	Regional RV akinesia, dyskinesia, or aneurysm and one of the following (end diastole): a) PLAX RVOT ≥ 29 mm to < 32 mm (PLAX/BSA ≥ 16 to <19 mm/m^2) b) PSAX RVOT ≥ 32 to < 36 mm (PSAX/BSA ≥ 18 to < 21 mm/m^2) c) Fractional area change > 33 to ≤ 40%
MRI	Regional RV akinesia, dyskinesia, or dyssynchronous RV contraction and one of the following a) Ratio RVEDV/BSA ≥ 110 mL/m^2 (male), ≥ 100 mL/m^2 (female) b) RVEF ≤ 40%	Regional RV akinesia, dyskinesia, or dyssynchronous RV contraction and one of the following: a) Ratio RVEDV/BSA ≥ 100 to < 110 mL/m^2 (male), ≥ 90 to 100 mL/m^2 (female) b) RVEF > 40 to ≤ 45%
RV angiography	Regional RV akinesia, dyskinesia, or aneurysm	
Tissue characterization of the wall		
Endomyocardial biopsy showing fibrous replacement of the RV free wall myocardium in more than one sample, with or without fatty replacement and with	Residual myocytes < 60% by morphometric analysis (or < 50% if estimated)	Residual myocytes 60% to 75% by morphometric analysis (or 50% to 65% if estimated)
Repolarization abnormalities		
ECG	Inverted T waves in the right precordial leads (V1–3) or beyond in individuals aged > 14 years (in the absence of complete RBBB QRS ≥ 120 ms)	I. Inverted T waves in leads V1–2 in individuals aged > 14 years (in the absence of complete RBBB) or in V4–6 II. Inverted T waves in leads V1–4 in individuals aged > 14 years in the presence of complete RBBB
Depolarization/conduction abnormalities		
ECG	Epsilon wave (reproducible low-amplitude signals between the end of the QRS complex to the onset of the T wave) in the right precordial leads (V1–3)	I. Late potentials using SAECG in more than one of three parameters in the absence of QRS duration ≥ 110 ms on the standard ECG: a) Filtered QRS duration (fQRS) ≥ 114 ms b) Duration of terminal QRS < 40 μV (low-amplitude signal duration) ≥ 38 ms c) Root-mean-square voltage of terminal 40 ms ≤ 20 μV II. Terminal activation duration of QRS ≥ 55 ms measured from the nadir of the S wave to the end of the QRS, including R' in V1–3 in the absence of complete RBBB

Arrhythmias		
	Nonsustained or sustained VT of LBBB with superior axis (negative or indeterminate QRS in leads II, III, aVF and positive in lead aVL)	I. Nonsustained or sustained VT or RV outflow configuration, LBBB morphology with inferior axis (positive QRS complexes in leads II, III, aVF and negative in lead aVL) or of unknown axis II. > 500 ventricular extrasystoles per 24 h (Holter)
Family history		
	I. ARVC confirmed in a first-degree relative who meets the current Task Force Criteria II. ARVC confirmed pathologically at autopsy or surgery in a first-degree relative III. Identification of a pathogenetic mutation categorized as associated or probably associated with ARVC in the patient under evaluation	I. History of ARVC in a first-degree relative in whom it is not possible or practical to determine whether the family member meets the current Task Force Criteria II. Premature sudden death (aged < 35 years) due to suspected ARVC in a first-degree relative III. ARVC confirmed pathologically or by the current Task Force Criteria in a second-degree relative

BSA: body surface area; ECG: electrocardiogram; echo: echocardiogram; MRI: magnetic resonance imaging; PLAX: parasternal long-axis; PSAX: parasternal short-axis; RBBB: right bundle branch block; RV: right ventricular; RVEDV: right ventricular end-diastolic volume; RVEF: right ventricular ejection fraction; RVOT: right ventricular out fl ow tract; SAECG: signal-averaged electrocardiogram; VT: ventricular tachycardia; aVF, aVF, augmented vector foot; aVL, augmented vector left

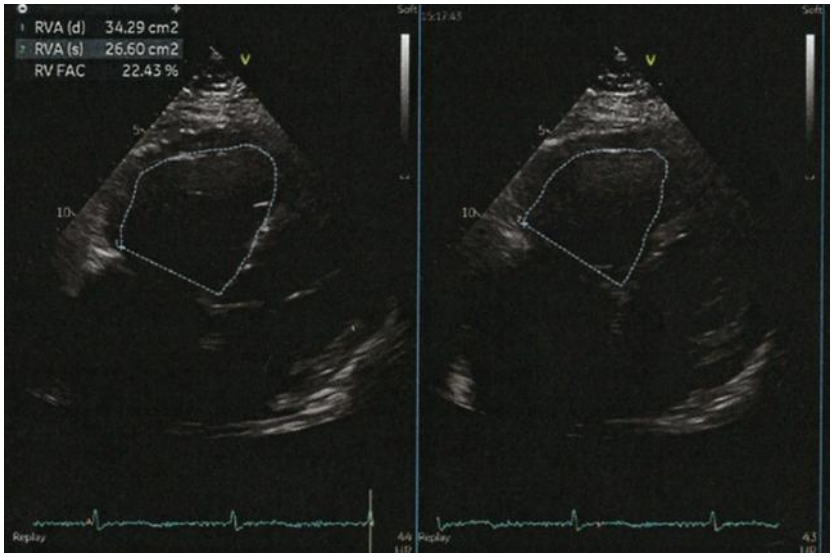

Fig. 3. Right ventricular fractional area change of 22.43% is seen on echocardiography

Approximately 2 years later, he was scheduled for elective open cholecystectomy. When he was admitted to the surgical ward, his ARVC was well-controlled. Total intravenous anesthesia, mainly remimazolam, was planned because of its limited hemodynamic effect. In addition to the usual ECG and oxygen saturation, monitoring was performed with an invasive intra-arterial pressure monitor and central venous catheter, and a defibrillation pad was applied to allow synchronized cardioversion/defibrillation as needed. In patients with ARVC, transesophageal echocardiography (TEE) should also be considered for monitoring during major and prolonged surgical procedures with significant blood loss [5,8]. TEE may also provide additional diagnostic information for patients with intraoperative cardiac arrest and may directly guide specific, potentially life-saving therapies [4]. The patient had stable ARVC and was unlikely to have major bleeding; therefore, TEE was only prepared for use at any time. We planned to administer phenylephrine and

noradrenaline for hypotension and atropine for bradycardia β-stimulants are not recommended in the presence of hypotension or bradycardia because β-stimulation is the most common cause of stable sustained VT [2,5,8]. General anesthesia was induced with remimazolam (12 mg/kg/h) and fentanyl (500 μg), and tracheal intubation was performed after the administration of rocuronium (1.0 mg/kg). The use of remimazolam helped maintain hemodynamic stability during anesthesia induction. Following intubation, anesthesia was maintained with remimazolam (0.5–1.0 mg/kg/h), remifentanil (0.1–0.2 μg/kg/min), rocuronium (7.0 μg/kg/min), and oxygen-in-air gas mixture. The bispectral index (BIS) was used to titrate the remimazolam dose, maintained at 40–60 throughout anesthesia.

After induction of general anesthesia, the modified thoracoabdominal nerves block perichondrial approach (m-TAPA) was performed as part of the multimodal analgesia protocol. Levobupivacaine (60 mL, 0.25%) was then administered. Acetaminophen 1,000 mg and fentanyl 150 μg were intravenously administered during skin closure. A total of 750 μg of fentanyl was administered. Hemodynamic stability was maintained intraoperatively, and catecholamine use was not warranted. The operative time was 154 min, and the anesthesia time was 265 min. There was no intraoperative hypotension, uncompensated blood loss, hypercarbia, hypoxia, or acidosis, which can induce cardiac arrhythmias with anesthetic management, and no VT or other arrhythmias. Muscle relaxation was antagonized by sugammadex, and remimazolam was antagonized by flumazenil. The patient was extubated in the operating room as he was fully awake, had adequate spontaneous respiration, and vital signs were stable. Remimazolam was used under BIS monitoring between 40 and 60 until before extubation; therefore, there was no intraoperative awareness. After the surgery, the patient did not complain of intraoperative awareness. The patient's numerical rating score (NRS) was 0/10 during the first 12 h of follow-up. No analgesic medication was administered within 48 h. "Little pain" was recorded in the clinical record at 24 h and "no pain" at 48 h. No episodes of stable sustained VT or other cardiovascular episodes were observed during the perioperative period. No serious adverse events, such as allergic reactions, local anesthetic systemic toxicity, pneumothorax, or uncontrollable persistent hypotension, were observed.

3. DISCUSSION

Sufficient anesthetic management during an open cholecystectomy of a patient with ARVC, with a history of recurrent stable sustained VT, was achieved. The patient received total intravenous anesthesia with remimazolam, fentanyl, remifentanil, and m-TAPA for postoperative analgesia. Although relatively rare, ARVC may cause sudden, unexpected deaths during the perioperative period [4]. When a β-stimulator is used, ARVC can increase the risk of arrhythmias, such as stable sustained VT [2,5]. Therefore, it is important to maintain hemodynamic stability to avoid the need for β-stimulants to prevent fatal arrhythmias during the perioperative period in patients with ARVC [5].

We considered which general anesthesia would be the preferred choice.

Thiopental has been shown to promote adrenaline-induced arrhythmias; therefore, general anesthesia with propofol or benzodiazepines is preferred [2,4,8]. In another report comparing remimazolam and propofol use in cardiac surgery, adrenaline, cortisol, and blood glucose levels measured 2 h after surgery were significantly lower in the remimazolam group [9]. Therefore, remimazolam reduces surgical hemodynamic changes and the surgical stress response. In addition, remimazolam is less likely to cause hypotension and requires less use of β-stimulators. Therefore, remimazolam may be the best choice for the anesthetic management of ARVC.

Remimazolam is a benzodiazepine agonist created as an ultra-short-acting anesthetic with a high affinity for the benzodiazepine-binding site of the γ-aminobutyric acid receptor and is metabolized by esterases. Remimazolam has a context-sensitive half-time of 6–7 min during its administration for various durations, and the elimination half-time of remimazolam is approximately 48 min [10,11]. Only angle-closure glaucoma is contraindicated.

Remimazolam can maintain hemodynamic stability, eliminating the need for catecholamines, but it has no effect on the β receptors themselves. As for catecholamines, α-adrenergic agonists, such as phenylephrine or noradrenaline, are preferred over β-adrenergic stimulators in patients with ARVC [2,5,8]. However, catecholamine use was not needed for this patient. In this case, atropine was

administered for bradycardia. Remifentanil, fentanyl, and rocuronium were administered safely [4,8]. Oh et al. reported that remimazolam at 0.35 mg/kg could induce loss of consciousness and did not cause significant hemodynamic depression [12]. Therefore, remimazolam alone may be sufficient to induce anesthesia without the use of remifentanil when hypotension should be avoided.

On the other hand, postoperative pain is associated with increased levels of endogenous catecholamines, which can lead to severe arrhythmia [2,5]. M-TAPA was used as postoperative analgesia. With the use of 60 mL of 0.25% levobupivacaine, the pain was NRS 0–1 12 h after surgery; thus, there was no need for additional analgesics.

β-blockers not only prevent ventricular arrhythmias but are also thought to be beneficial in the management of patients with heart failure [13-15]. If a patient is being actively treated with β-blockers for ARVC, they should continue to undergo β-blockers perioperatively and should be administered their usual dose the morning of the surgery [4]. β-blocker such as landiolol or esomolol should be available for suppression of VT, if they occur [8].

Prior to elective surgery, patients should be clinically optimized with pharmacologic or invasive treatment [8], and the surgery should be postponed until the arrhythmia and symptoms are controlled [4,5]. Emergency surgery should be avoided in situations where ARVC is unstable. In this case, surgery was performed approximately 2 years after the onset of VT. During this time, no VT occurred, and the ARVC was well-controlled.

Though ARVC appears to be a major cause of sudden and unexpected perioperative death, to the best of our knowledge, there are no published reports on the incidence of ARVC during the perioperative period [4]. A French autopsy report found ARVC in 18 (36%) of 50 sudden perioperative deaths [16]. No preoperative cardiac, intraoperative anesthetic, or surgical complications were observed in the 18 ARVC cases. This autopsy report has some limitations. The percentage of cases in the actual number of anesthesia management cases was not shown, preoperative ECGs were not presented, family history was not described, and there were regional and racial differences in the prevalence of ARVC. Anesthesiologists should pay special attention to ARVC because of the high risk of VT and sudden death during the perioperative period despite the above-mentioned limitations.

Among the diagnostic criteria for ARVC, the most frequently described ECG finding are T wave inversions in V1–3 [15,17]. T wave inversion in V1–3 in those aged > 14 years is seen in only 4% of women and 1% of men and is a useful sign in this patient group [5-7]. If T wave inversion is observed in V1–3 in a young patient, further evaluation, such as echocardiography, may be considered [2,5]. In the future, it would be desirable to investigate the sensitivity in the diagnosis of ARVC in cases with V1–3 T wave inversion on routine preoperative ECGs. The epsilon wave observed in this case was inappropriate for screening because it was observed in only 30% of the patients with ARVC [18].

A limitation of this case report is that there was only one case. Further studies are needed to determine whether remimazolam is the best choice for anesthesia in patients with ARVC.

4. CONCLUSION

We report a case of ARVC that was safely managed using total intravenous anesthesia with remimazolam. Although ARVC is a rare heart disease, it may cause sudden death during the perioperative period and should be managed promptly and appropriately. Anesthesiologists should pay close attention to anesthetic management in patients with ARVC.

CONSENT

Written informed consent was obtained from the patient (or other approved parties) for the publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. This report has been approved by the Nagasaki Rosai Hospital Institutional Review Board (No.05001, 2023/04/14).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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