Automation of Mechanical Ventilation

Richard D. Branson, MSc, RRT, FCCM

KEYWORDS

• Intensive care unit • Mechanical ventilation • Closed loop ventilation • Weaning

KEY POINTS

- Mechanical ventilation is ubiquitous to intensive care.
- Mechanical ventilation has the potential for harm and management by experienced clinicians is mandatory.
- Automated control of ventilation may provide some advantages related to consistency of care and maintaining evidenced based protocols.

INTRODUCTION

Mechanical ventilation is ubiquitous to intensive care. In fact, the foundation of intensive care units (ICUs) can be traced to housing patients requiring mechanical ventilation for specialized care. In the past 2 decades, our understanding of mechanical ventilation and its complications has become steeped in evidence and physiology. After nearly 60 years of modern positive pressure ventilation, it seems that mechanical ventilation has a fairly narrow therapeutic index between the effective and lethal dose. Clearly, the impact of tidal volume (V_T) and airway pressures on ventilator-induced lung injury and mortality are firmly established.[1]

Yet, even in the presence of evidenced-based guidelines,[2] clinicians routinely ignore even the best proven strategies.[3] The complexity of mechanical ventilation and of ventilators has done little to improve this reality. Clinicians are influenced by local champions, manufacturers, and mentors. This is frequently manifest in the way individuals describe ventilation techniques by the proprietary names of devices, versus by function. In the face of this conundrum, the failure of trained clinicians to adopt evidence-based practices, automation of ventilation settings could provide a solution. However, this remains to be proven. This article reviews the evidence regarding the use of automated control of mechanical ventilation.

Division of Trauma and Critical Care, University of Cincinnati, 231 Albert Sabin Way #558, Cincinnati, OH 45267, USA
E-mail address: Richard.branson@uc.edu

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DEFINITIONS

A closed loop control describes a system that changes its output based on a desired input. These systems are also referred to as feedback control systems. In the most basic forms, closed loop control is part and parcel of every mechanical ventilation system. Pressure support uses the pressure signal as a target and controls flow to reach and maintain the desired pressure. This is accomplished by a rapid initial flow followed by a quickly decelerating flow pattern. Wysocki and colleagues[4] have classified closed loop systems based on the level of sophistication into simple, physiologic signal based, and explicit computerized protocols (ECP). **Table 1** provides examples of these 3 types of closed loop systems.

A simple closed loop system includes pressure support or pressure control ventilation. A physiologic signal-based system would include neurally adjusted ventilatory assist (NAVA) or proportional assist ventilation. In these examples, output is increased or decreased in proportion to the input signal. In the case of NAVA, the pressure applied is proportional to the integral of the electrical activity of the diaphragm. Thus, as patient effort increases and electrical activity of the diaphragm is greater, the level of assistance is greater.[5]

Table 1
Classification of closed loop systems based on sophistication

Control	Example	Output	Input(s)	Comments
Simple	Pressure support ventilation	Flow	Airway pressure	
Physiologic signal based	NAVA	Pressure	EAdi	Delivered instantaneous airway pressure is proportional to the integral of the EAdi. During NAVA, the breath is triggered and cycled based on EAdi. The airway pressure applied by the ventilator is determined as: Airway Pressure = NAVA level × EAdi, where airway pressure (cm H_2O), EAdi is the instantaneous integral of the diaphragmatic electrical activity signal (μV), and the NAVA level (cm H_2O/μV) is a proportionality constant set by the clinician.
Explicit computerized protocol	SmartCarePS	Pressure	Delivered V_T Respiratory frequency End tidal CO_2	Smart care uses a number of clinician inputs to alter ventilator operation. The range of acceptable ventilation can be altered in the presence of COPD or neurologic injury. Additionally, the choice of 'night rest', prevents weaning during selected overnight hours.

Abbreviations: CO_2, carbon dioxide; COPD, chronic obstructive pulmonary disease; EADi, electrical activity of the diaphragm; NAVA, neurally adjusted ventilatory assist; V_T, tidal volume.

An ECP is medical knowledge resident in technology, applied to specific decision making for an individual patient at a particular point in time.[4] ECP systems may use multiple inputs to control a single ventilator output (pressure support level in SmartCarePS) or multiple inputs to control several ventilator outputs as seen with Intellivent adaptive support ventilation (iASV).[6,7] The rules in an ECP can include a series of, "if…, then" statements. For example, during closed loop control of inspired oxygen, "*if* oxygen saturation from pulse oximetry (SpO_2) is less than 90% *then* increase the inspired oxygen concentration (Fio_2) by 0.05." These "if… then" statements can become similar to decision making by clinicians, taking into account the difference between the SpO_2 target and the measured value, the number of hypoxemic events in the last hour and the stability of SpO_2, to alter the interval if Fio_2 adjustment. As an example, if the difference between the actual and target SpO_2 is 10% the adjustment in Fio_2 might be 0.10 every 30 seconds compared with an SpO_2 difference of 2%, resulting in a change in Fio_2 of 0.02 every 30 seconds. During SmartCare PS, the change in pressure support level varies based on the desired respiratory frequency, end-tidal carbon dioxide ($ETCO_2$), and V_T. The range of acceptable values for these variables can be altered by the clinician for a given patient in the setting of chronic obstructive pulmonary disease (COPD) or neurologic injury. In the former, the acceptable $ETCO_2$ is higher, whereas in the latter the range of $ETCO_2$ is lower. In this manner, the ventilator is making decisions based on individual patient characteristics, just as the caregiver might.

Chatburn and associates[8] have proposed a more complex system for describing mechanical ventilator operation during traditional and closed loop control. This classification uses 7 separate terms for describing the targeting schemes for ventilator modes. These include set point, dual, servo, adaptive, biovariable, optimal, and intelligent.[8] Aside from the added complexity, the use of engineering terms, although consistent with the literature, also seems to infer a value judgment. For instance, intelligent implies a system that is, perhaps, superior to optimal. In some ways, however, this is also a system that is based on increasing sophistication. Evidence is required to in fact conclude that intelligent is superior to set-point targeting. In fact, the use of volume control, continuous mandatory ventilation, a set-point targeting scheme is the only method to date that has demonstrated an impact on outcome. That being the control of V_T during ventilator support of acute respiratory distress syndrome.[9]

PROPOSED ADVANTAGES

Closed loop control is thought to offer a number of advantages compared with traditional physician control of mechanical ventilation. The sheer number of physiologic variables available to the bedside clinician is daunting. Coupled with the dozens of clinical decisions that must be made daily, the opportunity for error is significant. Despite our best efforts, the ability of the human mind to deal with this volume of information is limited.[10] Staffing shortages, long hours, and overnight shifts only serve to compound these issues.

The implementation of closed loop control may help to relieve the burden of decisions by maintaining ventilation and oxygenation in prescribed ranges while adhering to lung protective rules.[4] Additional advantages could include reduced costs, provision of appropriate care in remote environments in the absence of experts, reduced practice variation, reduced weaning times, and implementation of evidence-based guidelines.[11]

AUTOMATED CONTROL OF MECHANICAL VENTILATION

Although closed loop control is available in a number of ventilator modes including PSV, PCV, NAVA, proportional assist ventilation, and adaptive pressure control,

the emphasis of this article is on the use of automated mechanical ventilation and, specifically, on the ventilation modes that adjust support to meet patient demand during maintenance ventilation and weaning. The techniques to be considered include adaptive support ventilation (ASV), iASV, and SmartCare PS.

ADAPTIVE SUPPORT VENTILATION

ASV is a closed loop mode of mechanical ventilation designed to titrate ventilator output on a breath-by-breath basis. The level of ventilatory support provided by the ventilator is determined by respiratory mechanics and breathing effort. The goal of ASV is to provide a preset level of minute ventilation while minimizing the work of breathing. Under normal conditions, the minute volume setting is set at 100% of a normal minute volume based on predicted body weight of 0.1 L/kg/min. Thus, a 70-kg patient would receive a minute ventilation of 7.0 L/min.

ASV adjusts the inspiratory pressure to achieve a respiratory pattern (V_T and frequency) that minimizes the work of breathing based on the Otis equation. Importantly, however, the range of available V_T is controlled by the maximum pressure setting selected by a clinician. Breaths alternate between pressure control and pressure support breaths based on the presence or absence of spontaneous breathing efforts. Conceptually, ASV can provide synchronized intermittent mandatory ventilation and PSV, but in this author's experience, breaths are either all mandatory or spontaneous. During mandatory breaths, ASV controls the inspiratory time and inspiratory:expiratory ratio (I:E) based on measurement of the expiratory time constant. Lower compliance results in a short I:E, whereas a high resistance results in a longer I:E to avoid air trapping. ASV requires the clinician set Fio_2 and positive end-expiratory pressure (PEEP).

ASV is a rule-based technique that guides the patient to achieve a minimum minute ventilation using an "optimal" breathing pattern. ASV uses "hard" and "soft" rules. Hard rules are preset limits unaffected by user input or patient mechanics. An example of a hard rule is the high-pressure limit. The ventilator will not exceed the pressure limit, despite failure to achieve other preset goals. Soft rules are determined by clinician input and respiratory mechanics. Soft rules generally have a range of operation and may change with time and clinician input. The details of ASV operation have been discussed extensively elsewhere.[12–17]

Clinical Studies of Adaptive Support Ventilation

ASV can be used to provide support during the initiation, maintenance, and weaning of mechanical ventilation. Each of these implementations have been studied in human subjects. These topics are considered separately.

ASV has been used in a number of studies evaluating time to discontinuation of ventilatory support after coronary artery bypass surgery.[18–23,25,26] Studying this large, relatively homogenous, readily available population is attractive on many levels. However, this population requires ventilation primarily as a "casualty of anesthesia" and under normal circumstances have minor lung injury.[27] In these 8 studies, the impact on duration of ventilation favors ASV in 4 instances and demonstrates no difference in 4 instances. **Table 2** describes the studies and outcomes. Of note, these studies find that ASV required fewer clinician/ventilator interventions, fewer arterial blood gases, fewer ventilator alarms, and a lesser incidence of postoperative atelectasis on radiographs.

There are several additional areas of concern with ASV in this environment. The first is related to the concept of automated weaning. To decrease the level of ventilator

Table 2
Clinical studies of ASV after cardiac surgery

First Author	Sample Size	Population	Comparator	Primary Outcome	Findings
Sulzer et al,[18] 2001	36	Uncomplicated fast track cardiac surgery	PSV	Duration of ventilation	ASV shorter duration of ventilation 3.2 h vs 4.1 h Fewer blood gases in the ASV group No difference in sedation requirements
Cassina et al,[19] 2003	155	Uncomplicated fast track cardiac surgery	None	Duration of ventilation	Duration of ventilation was 3.6 h V_T was 8.7 $\pm$ 1.4 mL/kg
Petter et al,[20] 2003	34	Uncomplicated "fast track" cardiac surgery	SIMV followed by PSV	Duration of ventilation	No difference in duration of ventilation 2.7 vs 3.2 h No difference in sedation requirements
Gruber et al,[21] 2008	48	Uncomplicated fast track cardiac surgery	AutoMode, PRVC, and volume support	Duration of ventilation	Shorter duration of ventilation with ASV 300 vs 540 min No difference in number of blood gases or ventilator manipulations
Dongelmans et al,[22] 2009	121	Non–fast track coronary bypass surgery	PCV followed by PSV	Duration of ventilation	No difference in duration of ventilation 16.4 h vs 16.3 h No difference in sedation requirements
Dongelmans et al,[23] 2010	126	Non–fast track coronary bypass surgery	ASV	Duration of ventilation	No difference in the duration of ventilation 10.8 h vs 10.7 h
Zhu et al,[24] 2015	53	Uncomplicated fast track cardiac valvular surgery	SIMV or SIMV + PSV	Duration of ventilation	Shorter duration of ventilation with ASV 205 min vs 342 min
Tam et al,[25] 2016	52	Uncomplicated fast track cardiac surgery	ASV at a constant V_E target vs ASV with a decremental V_E target	Duration of ventilation	Shorter duration of ventilation with decremental ASV 145 min vs 309 min No difference in adverse events
Moradian et al,[26] 2017	115	Uncomplicated fast track cardiac surgery	ASV vs SIMV + PSV	Duration of ventilation	No difference in duration of ventilation Fewer alarms and caregiver interactions with ASV

Abbreviations: ASV, adaptive support ventilation; PCV, pressure control ventilation; PRVC, pressure regulated volume control; PSV, pressure support ventilation; SIMV, synchronized intermittent mandatory ventilation; V_E, minute ventilation; V_T, tidal volume.

assistance, the clinician must decrease the target minute volume. This approach seems to facilitate faster ventilator discontinuation. However, the requirement for clinician intervention, adds an "open loop" to the closed loop system. Choosing the appropriate minute volume target has not been extensively studied and requires some elucidation.[25,28,29] The selected V_T during ASV can exceed lung protective limits and the potential for ventilator-induced lung injury after surgery is a concern.[30]

Several recent trials have evaluated ASV for weaning in patients with acute respiratory failure. Chen and colleagues[31] reported their experience with ASV in a 16-bed Chinese ICU staffed by a single respiratory therapist during the day and no coverage at night. They compared the management of patients with ASV with a matched historical control using synchronized intermittent mandatory ventilation and PSV. Under these rather unique circumstances, the authors demonstrated that patients in the ASV group achieved extubation readiness within 1 day of enrollment more often, achieved weaning within 21 days. However, there were no differences in the duration of ICU or hospital stay. These findings must be considered in light of this unique staffing model. However, a potential advantage of closed loop ventilation is the ability to continue care in the absence or unavailability of caregivers. This study seems to support this thesis.

Kirakli and colleagues[32] compared ASV with PSV for weaning in patients with COPD. They found that patients ventilated with ASV had shorter weaning times and equivalent weaning success. However, the total duration of ventilatory support did not change. The use of ASV for weaning after recovery from acute respiratory failure and after liver transplantation has been reported.[31,33]

ASV has been used successfully as a primary mode of ventilator support during acute respiratory failure. The algorithm based on an expiratory time constant was shown to set I:E and respiratory frequency appropriately for both obstructive and restrictive disease. These reports find a reduction in manual ventilator adjustments, similar gas exchange, and perhaps improved CO_2 elimination for a given combination of V_T and respiratory frequency.[34–36] Patients with obstructive disease in these trials, however, can receive V_Ts outside suggested lung protective values.

One criticism of ASV has been the finding that the V_T may approach 9 to 10 mL/kg in some patients.[30,37–39] This limitation can be overcome by appropriate setting of the maximum pressure and V_T limits. ASV has been commercially available for more than 20 years and widespread adoption has not occurred. Although ASV may facilitate weaning when the percent of minute volume value is appropriately set, it seems to have no clear advantage over manual techniques. Closed loop techniques can decrease practice variation through appropriate selection of hard rules, such a maximum pressure chosen by the operator. This author has previously argued that techniques like ASV may provide the greatest benefit in resource-limited environments, and the work by Chen and colleagues[31] seems to support this opinion.

Intellivent Adaptive Support Ventilation

Intellivent ASV is the logical extension of ASV to include the automated selection of Fio_2 and PEEP. The PEEP/Fio_2 controller uses the PEEP tables from the ARDS Network' s prospective randomized multicenter trial of 6 mL/kg versus 12 mL/kg V_T for the treatment of acute lung injury and acute respiratory distress syndrome (ARMA) and the ARDS Network's prospective randomized multi-center trial of higher end-expiratory lung volume/lower Fio_2 versus lower end-expiratory lung volume/higher Fio_2 ventilation in acute lung injury and acute respiratory distress syndrome (ALVEOLI).[38] The ARMA trial used an aggressive Fio_2 strategy, whereas the ALVEOLI trial is PEEP intensive. An integral pulse oximeter provides the input signal to the ventilator, where the clinician can set the desired SpO_2. Pulse volume variability from the

oximeter can also provide information regarding patient hemodynamic status, limiting the use of PEEP in favor of Fio_2 during hemodynamic compromise. Intellivent is currently not commercially available in the United States.

The minimum PEEP is 5 cm H_2O, and at initiation the controller uses the ARMA PEEP/Fio_2 table to reach the desired SpO_2. After stabilization the Fio_2 and PEEP, patients are weaned using the ALVEOLI table. **Fig. 1** provides a pictograph of the PEEP/Fio_2 tables used during Intellivent.

Clinical studies of Intellivent adaptive support ventilation

The use of iASV has been limited owing to the recent introduction and unavailability in the United States. In a preliminary trial of sedated patients with acute respiratory failure, Arnal and colleagues[7] demonstrated that, during a 2-hour crossover trial, iASV provided ventilation at a lower airway pressure, volume, and Fio_2 while producing the same results in terms of oxygenation compared with ASV. The V_Ts were slightly lower with iASV and $Paco_2$ higher. In a follow-up crossover trial, iASV applied for 24 hours compared with PSV demonstrated improved oxygenation. In this study, PEEP was higher and more variable during iASV, as might be expected.[40] The authors suggest that the biovariability of PEEP might explain the improved oxygenation.

Arnal and colleagues applied iASV in a wide range of patient populations ventilated for less than 24 hours and found that ventilator settings were selected appropriately based on the lung condition, particularly in passive patients. However, like traditional ASV, spontaneously breathing subjects (breathing with adaptive pressure support) have less variability in volume and pattern.[41] A randomized trial

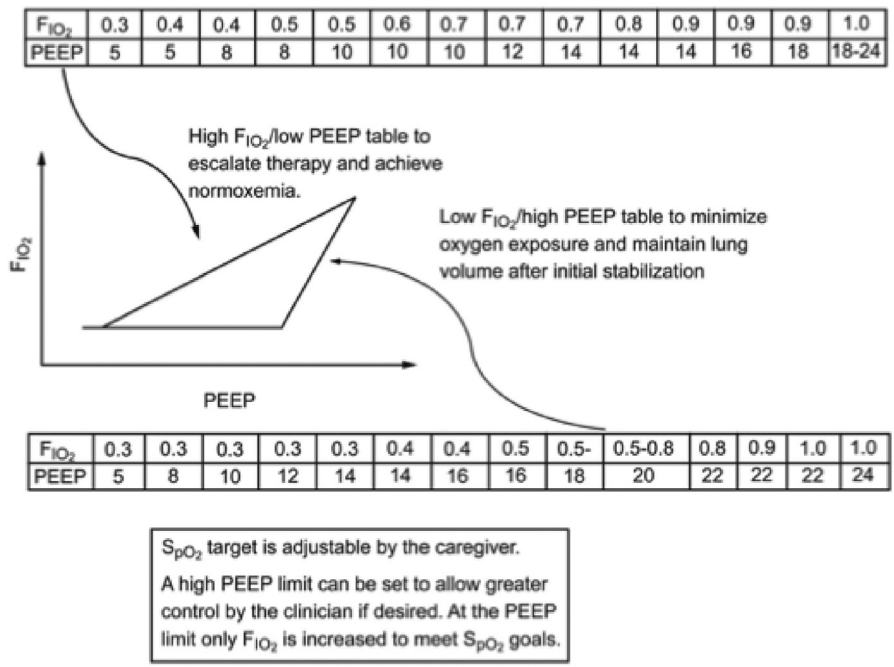

Fig. 1. Combination of the positive end-expiratory pressure (PEEP)–fraction of inspired oxygen (FIO_2) tables from the ARDSnet ARMA and ARDSnet ALVEOLI trials used for increasing and decreasing oxygenation support during Intellivent adaptive support ventilation (iASV). SpO_2, oxygen saturation. (*From* Branson RD. Modes to facilitate ventilator weaning. Respir Care 2012;57:1642; with permission.)

of iASV compared safety and efficacy with modes chosen by the attending physician as the time spent within previously defined ranges of nonoptimal and optimal ventilation. Interestingly, iASV was more likely to be in the suboptimal range for maximum pressure. As in previous trials, iASV made more manipulations but required fewer clinician interactions and the variability of volumes and airway pressures were greater.[42]

Fot and colleagues[43] evaluated iASV compared with protocolized weaning and synchronized intermittent mandatory ventilation plus PSV after coronary bypass grafting. They found that iASV and protocolized weaning had similar outcomes and shortened weaning compared with traditional methods. The authors noted the decrease in clinician interactions with the ventilator, but no other advantages. More recently, Arnal and associates compared iASV with either PSV or volume control, continuous mandatory ventilation in 60 subjects. They concluded that iASV decreases the number of manual ventilator setting changes with no difference in the number of arterial blood gas analyses or sedation use. Using a Likert scale, caregivers rated iASV as easier to use compared with conventional ventilation modes.[44]

SmartCARE PS

SmartCarePS describes control of PSV where the pressure support level is based on the patient's V_T, respiratory frequency, $ETCO_2$, and a series of preset parameters based on the patient condition (presence of COPD or neurologic injury). SmartCarePS adjusts pressure support to maintain the patient in a "normal" range of ventilation. A normal range of ventilation is typically defined as a V_T of 300 mL, a respiratory frequency between 12 and 30 breaths/min, and an $ETCO_2$ of less than 55 mm Hg (these settings can be adapted for subjects with COPD or neurologic injury). Outside of the normal range, SmartCarePS defines other conditions and manipulates the pressure support based on the current value, the clinician input parameters, and the patient's historical breathing pattern. SmartCarePS is intended for weaning and, therefore, not used clinically for the support of acute respiratory failure.[11]

Clinical studies of SmartCare PS

Introduced in 1996, SmartCare PS has been evaluated in a number of weaning trials.[6,45–51] The original trial simply compared the duration of ventilation in the specified ranges of comfort compared with clinician-selected PSV. This study found that SmartCarePS maintained patients in the desired ranges far more frequently.[45] Lellouche and coworkers[47] published the first and largest randomized trial compared with traditional weaning in 5 European centers in 2006. This report found significantly quicker weaning times with SmartCarePS compared with traditional weaning. However, in at least 2 centers, spontaneous breathing trials were not used in the control arm.[47] This is a limitation of the study, but represents a pragmatic trial. Across the world, the use of protocolized weaning is espoused by clinical practice guidelines[52] but not routinely implemented.

Subsequent trials of SmartCarePS have found both advantages and no advantage compared with traditional weaning based on patient condition (sepsis vs COPD vs cardiac surgery), the type and staffing of the ICU, and patient age (adults vs pediatrics).[48–51] Cochrane reviews of automated weaning routinely find that automated weaning demonstrates approximately a 30% reduction in weaning time compared with traditional weaning. However, lack of standards in the control arm of trials, heterogeneity, and small numbers limit the strength of these conclusions.[53] Large multicenter trials are needed to determine the value of SmartCarePS in routine care.

Concerns with the Automated Control of Ventilation

Automation of mechanical ventilation has a number of advantages, as described. The potential disadvantages are less frequently discussed, but require additional research. As an example, if the ventilation system increases PEEP and or Fio_2 rapidly in response to hypoxemia and prevents the typical desaturation events that routinely alert caregivers to worsening lung function, this event must be communicated to the staff. Increases in PEEP and airway pressures that may result in hemodynamic compromise also require additional safety measures. As clinicians, we consider heart rate, blood pressure, filling pressures, vasopressor therapy, and fluid status during the manipulation of mean airway pressures. At present, no ventilation system has the ability to include these additional inputs into the ventilator decision process. It may be that limiting changes in PEEP to less than 12 cm H_2O is needed and increases beyond this value approved by the clinician with knowledge of hemodynamic performance and current therapy.

As seen with several of these techniques, certain situations can result in excessive V_T and pressure delivery, perhaps leading to ventilator-induced lung injury. Alarm settings and alert settings require additional care.

SUMMARY

Simple closed loop control of mechanical ventilation is routine and operates behind the ventilator interface. More complex systems described as intelligent control or ECP, are commercially available but have yet to gain widespread acceptance.[54] New trials demonstrating a cost benefit of automated ventilation are required. Simply reducing the number of caregiver interactions is neither an advantage for the patient or the staff. In fact, automated systems causing lack of situational awareness of the ICU are a concern. Along with these autonomous systems must come monitoring and displays that easily inform the staff of the patients current condition and response to therapy. Alert notifications for sudden escalation of therapy are required to ensure patient safety.

The use of automated ventilation clearly has utility in remote settings in the absence of experts. There are more than 1000 critical access hospitals in the United States, most with fewer than 50 beds that are the entry point to the health care system in rural America. These hospital lack ICUs and ICU and respiratory care expertise. Remote care in disaster and military medicine is another area where local expertise may not match the severity of patient illness. These environments represent a natural fit for automated ventilation. However, the cost and size of devices require modification.

Whether automated ventilation will be accepted in large academic medical centers remains to be seen. Despite staffing shortages and increased patient acuity, this author has never heard the ICU staff express that the solution to current concerns in the ICU is more automation of ventilator support.

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