Predictive factors for successful INTELLiVENT-ASV® use: A retrospective observational study

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Abstract

Background: INTELLiVENT-ASV® (I-ASV) is a closed-loop ventilation mode that automatically controls the ventilation settings. Although a number of studies have reported the usefulness of I-ASV, the clinical situations in which it may be useful have not yet been clarified. We aimed to report our initial 3 years of experience using I-ASV, particularly the clinical conditions and the technical and organizational factors associated with its use. Furthermore, we evaluated the usefulness of I-ASV and determined the predictive factors for successful management with I-ASV.

Methods: This single-center, retrospective observational study included patients who were ventilated using the Hamilton G5® ventilator (Hamilton Medical AG, Rhäzüns, Switzerland) from January 2016 to December 2018. The patients were categorized into the "I-ASV success" group and "I-ASV failure" group (those receiving mechanical ventilation with I-ASV along with any other mode). Multivariate analysis was performed to identify factors associated with successful I-ASV management.

Results : Of the 189 patients, 135 (71.4%) were categorized into the I-ASV success group. In the I-ASV success group, the reasons for ICU admission included post-elective surgery (94.1%), post-emergent surgery (81.5%), and other medical reasons (55.6%). The main reasons for not using I-ASV included strong inspiratory effort and asynchrony. The Acute Physiology and Chronic Health Evaluation (APACHE) II score was an independent predictive factor for successful management with I-ASV, with an odds ratio of 0.92 (95% confidential interval 0.87–0.96, $P = 0.0006$). The area under the receiver operating curve for the APACHE II score was 0.722 (cut-off: 25).

Conclusions : In this study, we found that 71.4% of the fully mechanically ventilated patients could be managed successfully with I-ASV. The APACHE II score was an independent factor that could help predict the successful management of I-ASV. To improve I-ASV management, it is necessary to focus on patient-ventilator interactions.

Background

INTELLiVENT-ASV® (I-ASV) is a closed-loop ventilation mode that automatically adjusts the ventilator settings of adaptive support ventilation (ASV). It automatically controls the fraction of inspiratory oxygen (F_IO_2), percentage minute ventilation (%MV), and positive end-expiratory pressure (PEEP) by using end-tidal carbon dioxide tension (E_TCO_2), respiratory rate, and arterial oxygen saturation of pulse oximetry (SpO_2) to keep the patient's lung ventilated safely. I-ASV can be managed using only one mode during the entire mechanical ventilation period, without pressure-controlled ventilation (PCV) or pressure support ventilation (PSV). The ASV algorithm is based on the minimal work and force of breathing [1], which is related with the minimal inspiratory pressure and tidal volume. Among the oxygen parameters, F_IO_2 and PEEP are adjusted automatically to reach a target SpO_2 and prevent over-oxygenation. Although several studies have reported the usefulness of I-ASV [2–7], the clinical situations in which it should be used have

not yet been clarified. Moreover, there are few experienced facilities where I-ASV can be used, and therefore, its usage status and efficacy have not been reported.

In our ICU, I-ASV was introduced in clinical practice in January 2016. In this study, we aimed to report our initial 3 years of experience with I-ASV, particularly the clinical conditions as well as the technical and organizational factors associated with its use. Moreover, we aimed to determine the associated factors in patients who could be ventilated successfully only with I-ASV.

Materials And Methods

Study design and setting

This was a single-center, retrospective, observational study conducted in the general intensive care unit (ICU) of a University Hospital (Tochigi, Japan). Patients who received mechanical ventilation (MV) using a Hamilton G5® ventilator (Hamilton Medical AG, Rhäzüns, Switzerland) (G5) in the ICU from January 2016 to December 2018 were included in this study. Clinical decisions to change the ventilation mode were made at the discretion of the attending ICU physicians. The study protocol was approved by the Institutional Research Ethics Committee of the Jichi Medical University Hospital (18–110). Informed consent was waived due to the retrospective nature of the study.

Participants

Patients were eligible for enrolment if they were (a) 20 years of age or older and (b) ventilated using the G5 during their ICU stay. Patients who were younger than 20 years of age or who were ventilated using other ventilators when starting MV were excluded from the study.

The baseline characteristics of the patients, including age, sex, height, body weight, body mass index (BMI), presence of sepsis, and type of ICU admission, were collected from the electronic medical records. The PaO_2/F_IO_2 (P/F) ratio on day 1, the use of continuous renal replacement therapy (CRRT), and the use of extracorporeal membrane oxygenation (ECMO) were also determined. The medical history, including the presence of end-stage renal function on hemodialysis and the hemi-lung status, was evaluated. Regarding ventilatory parameters, the type of ventilation mode, F_IO_2, PEEP, and %MV were evaluated during MV, along with the duration of MV. When appropriate, the reason for changing from I-ASV to a different ventilator mode was determined from the electronic medical records. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score [8] was used to assess the severity of each patient's illness. The mortality rates during the ICU stay were also evaluated.

In our ICU, the I-ASV is the first-choice mode of ventilation for all patients connected to a Hamilton G5 ventilator. Cases mainly ventilated in the I-ASV mode (apart from brief phases) were considered I-ASV successes. Brief phases of I-ASV switch-off were attributed to (a) PCV immediately after tracheal

intubation, (b) PSV for a manual spontaneous breathing trial (SBT) although I-ASV succeeded SBT automatically, and (c) a lack of medical staff experience with I-ASV (e.g., the activation of SpO_2 and E_TCO_2 sensors on the G5). In the absence of physicians experienced with I-ASV, our clinical protocols allowed physicians without these specific skills to switch off this advanced mode and use a conventional mode. In such cases, I-ASV was re-started as soon as possible. Brief phases of I-ASV switch-off were defined as periods of < 24 h in a conventional mode before switching back to I-ASV. Patients who did not meet that criterion were classified into the I-ASV failure group, which also included patients who did not receive I-ASV during MV.

Statistical analysis

All analyses were performed using JMP 14 pro (SAS Institute Inc., Cary, NC, USA). Data are presented as medians and interquartile ranges (25th − 75th percentiles) or as percentages. P-values < 0.05 were considered statistically significant. Categorical variables were compared between groups using Fisher's exact test, Student's t-test, and the Pearson chi-square test. The subgroup analyses were performed according to the type of ICU admission (post-elective surgery, post-emergency surgery, and medical reasons) and degree of hypoxemia (P/F < 100, 100–200, 200–300, and > 300). To evaluate the factors associated with successful management using I-ASV, a logistic regression analysis was performed to determine the non-adjusted and adjusted odds ratios (ORs) using a model based on age, sex, BMI, presence of sepsis, end-stage renal function on hemodialysis, P/F ratio, and APACHE II score. A forward stepwise elimination process was used to remove non-significant variables from the model. Using the area under the receiver operating characteristic curve (AUROC), we assessed the ability of each independent factor to predict successful ventilation with I-ASV [9].

Results

Enrolment and baseline characteristics

A total of 202 patients who received MV with G5 were enrolled in the study (Figure 1). Thirteen patients had been ventilated with other ventilators when starting MV. One hundred and thirty-five patients (71.4%) were classified into the I-ASV success group, and 54 (28.6%) were categorized into the I-ASV failure group. In the I-ASV success group, some patients had briefly received another ventilation mode for reasons such as PCV immediately after tracheal intubation (n = 5, 3.7%), PSV for manual SBT although I-ASV revealed SBT success (n = 7, 5.2%), and a lack of medical staff experience with I-ASV (n = 9, 6.7%).

Table 1 compares the characteristics of patients in the I-ASV success and I-ASV failure groups. I-ASV failure was associated with a high APACHE II scores (21 vs. 26, $P < 0.0001$), CRRT (10.4% vs. 44.4%, $P < 0.0001$), type of ICU admission ($P < 0.0001$) and low P/F ratio (278 vs. 167, $P < 0.0001$). Additionally, the duration of MV (5 vs. 10 days, $P < 0.0001$), length of ICU stay (6 vs. 11 days, $P < 0.0001$), MV after ICU (i.e.,, continued MV after ICU discharge, such as in the general ward or at a transferred hospital; 9.6% vs.

22.2%, *P* = 0.031), and ICU mortality (1.5% vs. 13.0%, *P* = 0.003) were all significantly lower in the I-ASV success group (Table 1).

Reasons for admission and severity of hypoxemia associated with the I-ASV success group

The reasons for ICU admission and the severity of hypoxemia were evaluated in the I-ASV success group. Notably, the I-ASV success group included 94% of the patients admitted for post-elective surgery, 81.5% of those admitted for post-emergency surgery, and 55.6% of those with other medical reasons. Regarding the severity of hypoxemia, 89.4%, 71.4%, 47.5%, and 35.0% of patients with a P/F ratio ≥ 300, 200 –300, 100 –200 and, <100, respectively, were classified into the I-ASV success group (Table 1).

Annual trends regarding successful I-ASV

The number of patients who were ventilated using the G5 increased annually. Among these patients, I-ASV was successful in 69.0% of patients in 2016, 72.1% in 2017, and 71.2% in 2018. Compared to patients in the I-ASV failure group, those in the I-ASV success group have lower APACHE II scores [19 vs. 27 in 2016 (*P* = 0.080), 17 vs. 23 in 2017 (*P* = 0.068), and 23 vs. 30 in 2018 (*P* < 0.0001)]. Based on the reasons for admission in 2018, 100% of those admitted for post-elective surgery, 90.6% of those admitted for emergent surgery, and 54.0% of those with other medical reasons (*P* = 0.0002) were classified into the I-ASV success group. Regarding the severity of hypoxemia in 2018, 92.3%, 75.0%, 52.6%, and 35.7% of patients with a P/F ratio of ≥ 300, 200–300, 100–200, and < 100, respectively (*P* = 0.0001), were classified into the I-ASV success group (Table 2).

Reasons for choosing other modes of ventilation

Figure 1 summarizes the reasons for choosing other modes of ventilation in the I-ASV failure group. The main reasons included patients' strong respiratory efforts (n = 10, 5.3%); asynchrony/tachypnoea (n = 9, 4.8%); abnormal respiratory patterns, including Cheyne-Stokes respiration and an opioid-induced respiratory pattern (n =7, 3.7%); unstable hemodynamic/metabolic acidosis (n = 5, 2.6%); severe respiratory failure/acidosis (n = 4, 2.1%); limitation of the ASV setting (n = 2, 1.1%); sensor problems (n = 2, 1.1%); other reasons (n=6, 3.2%); difficult indications (n = 9, 4.8%), such as ECMO (n = 4, 2.1%), pneumothorax (n = 3, 1.6%), one lung and hemiventilation (n = 2, 1.1%).

Multivariate analysis, ORs, and AUROC predictive of successful I-ASV

Among the seven evaluated parameters, the APACHE II score (OR: 0.92; 95% CI: 0.87– 0.96; *P* = 0.0006) was found to be an independent predictor of successful I-ASV. The AUROC for the APACHE II score was 0.722 (0.636–0.793, cut-off: 25 [sensitivity: 0.65, specificity: 0.67]) (Table 3 and Figure 2).

Discussion

We found that 71.4% of the evaluated patients were ventilated in the I-ASV mode throughout their ICU stay. The I-ASV success group included more than 90% of the patients undergoing post-elective surgery

but only 55.6% of those with other medical reasons. The main reasons cited for switching to other modes of ventilation were asynchrony and a strong patient inspiratory effort. Moreover, we identified the APACHE II score as a significant independent predictor of successful ventilatory management using I-ASV.

Our findings also demonstrated that in cases with few or no lung problems, ventilatory management almost exclusively with I-ASV was possible. Several studies have demonstrated the usefulness of I-ASV. Arnal et al. [2] reported that compared to ASV, I-ASV is safer and can provide ventilation with a lower pressure, volume, and F_IO_2 in passive patients with acute respiratory failure. In addition, Lellouche et al. [5] reported the safety of I-ASV for maintaining an optimal range of respiration in post-cardiac surgery patients. A randomized controlled trial that aimed to compare the efficacy of I-ASV with conventional ventilation methods in critically ill patients [7] found the I-ASV to be a safe and effective option in terms of the tidal volume, respiratory rate, SpO_2, and E_TCO_2. However, these studies were performed for short durations and did not evaluate the long-term success rates of I-ASV. Therefore, our study is the first to evaluate the long-term success of I-ASV in a real clinical situation.

In this study, the APACHE II score was an independent predictive factor for successful I-ASV. In addition, the cut-off value for the APACHE II score was 25. These results suggest that in cases of moderate to severe acute respiratory distress syndrome (ARDS) or severe multi-organ dysfunction, management by I-ASV alone may not be possible. In this study, we found that strong respiratory drive is one of the reasons for discontinuation of I-ASV. There is a possibility that high APACHE II scores are related to strong respiratory drive and I-ASV failure. However, such cases comprise relatively small proportions of exclusively mechanically ventilated patients. The LUNG SAFE study [10] reported that although approximately 33% of mechanically ventilated patients had acute hypoxic respiratory failure, only 13% of them had moderate or severe ARDS. In addition, when compared to other conventional ventilation methods, I-ASV is expected to reduce the burdens on medical staff members (e.g., physicians and nurses) because of the automation. Although there is little evidence regarding the reduction in medical staff workloads, I-ASV might be a better choice for the majority of mechanically ventilated patients.

I-ASV may be difficult to manage in some cases because of the strong respiratory effort required in patients with moderate to severe hypoxemia and respiratory/metabolic acidosis. A strong respiratory effort frequently requires high minute ventilation. As I-ASV has a setting limitation of 200% of 100 mL/predictable body weight, ventilated patients who require high minute ventilation might find I-ASV to be challenging. Moreover, ventilation with I-ASV during a high inspiratory flow rate becomes difficult due to asynchrony. In such cases, it is important to switch to an appropriate ventilation mode rather than continue with I-ASV. In this study, there were a few cases in which the trigger for spontaneous inspiration was suppressed by changing to PCV. Furthermore, in such situations, the use of narcotics such as morphine, sedatives, or muscle relaxants should be considered.

Our study had several limitations. First, this was a single-center, retrospective, observational study. Further studies are warranted to validate our findings. Second, there was a selection bias due to the specific choice of the G5. In our ICU, the G5 is preferred in cases of hypoxemia and severe organ dysfunction

rather than in cases involving post-elective surgery, and this preference could have influenced the success rate of I-ASV. If the number of post-elective surgery patients exceeded the number of patients with hypoxemia and severe organ dysfunction, it could have increased the success rate of I-ASV. Third, we did not correct ventilatory parameters such as the tidal volume, driving pressure, and PEEP. Therefore, we are unable to conclude whether I-ASV was superior to other conventional ventilator modes in this study. We are currently conducting a prospective study (UMIN000034417) to evaluate the usefulness of I-ASV relative to other conventional ventilation modes. Fourth, we did not record the types of asynchronies in detail. Hence, further studies are required to evaluate the types of asynchronies that increase the difficulty of respiratory distress management with I-ASV. Fifth, we did not have objective parameters for high respiratory efforts, like esophageal pressure. Finally, since the proficiency of medical staff with the I-ASV mode varies, our results might differ from those of other high-volume centers. However, this study included the first 3 years of experience with I-ASV in our ICU, and therefore our results may be useful with respect to the initial use of I-ASV.

Despite these possible limitations, our findings demonstrate that I-ASV is useful, especially for post-elective surgery patients and patients who do not have severe hypoxemia or severe organ dysfunction. Accordingly, it is important to select patients carefully for MV with I-ASV.

Conclusions

In this study, 71.4% of the patients could be ventilated with I-ASV, which included more than 90% of patients with post-elective surgery, but only 55.6% of those admitted for other medical reasons. Moreover, the APACHE II score was an independent factor predictive of successful management with I-ASV. The main reasons for an inability to ventilate exclusively with I-ASV included a strong inspiratory effort and asynchronies. A focus on patient-ventilator interactions is necessary to improve I-ASV management.

Declarations

Ethics approval and consent to participate: The study protocol was approved by the Institutional Research Ethics Committee of the Jichi Medical University Hospital (18-110). Informed consent was waived due to the retrospective nature of the study.

Consent for publication:

Availability of data and materials:

Competing Interests: SK has a contract of consultation with Hamilton Medical. A Hamilton G5 ventilator was lent out from Nihon Kohden.

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Author' contributions: SK designed the study and performed the statistical analysis; SK and SN interpreted the data and wrote the manuscript; and KT, KK, and JS contributed to the interpretation of data. All authors read and approved the final manuscript.

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Abbreviations

I-ASV**:** INTELLiVENT-ASV, Acute Physiology and Chronic Health Evaluation: APACHE, Continuous renal replacement therapy: CRRT, Extracorporeal membrane oxygenation: ECMO, Area under the receiver operating characteristic curve: AUROC, BMI: Body mass index, CKD on HD: chronic kidney disease on hemodialysis, ICU: intensive care unit, MV: mechanical ventilation, PaO_2/F_IO_2 ratio, P/F ratio.

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Tables

Table 1. Patient characteristics

	All patients	I-ASV success	I-ASV failure	*P*-value
	(n=189)	(n=135)	(n=54)	
Age, years	65 (52–74)	65 (50–74)	65 (54–74)	0.555
Sex, male	52.9%	50.4%	59.3%	0.333
Height, cm	160 (153–167)	159 (153–165)	162 (153–169)	0.160
Weight, kg	58 (50–67)	58 (51–67)	59 (50–68)	0.448
BMI, kg/m^2	22.6 (20.7–25.8)	22.6 (20.8–25.3)	22.5 (19.9–27.3)	0.798
APACHE II	23 (17–27)	21 (15–26)	26 (21–34)	<.0001
Presence of infection	52.9%	49.6%	61.1%	0.197
CKD on HD	6.9%	5.9%	9.3%	0.525
CRRT	20.1%	10.4%	44.4%	<.0001
Reasons for admission				<.0001
- Elective surgery		94.1% (32)	5.9% (2)	
- Emergent surgery		81.5% (53)	18.5% (12)	
- Medical reasons		55.6% (50)	44.4% (40)	
P/F ratio	252 (174–334)	278 (206–366)	167 (98–246)	0.0003
P/F ratio classification				<.0001
≥300		89.4% (84)	10.6% (10)	
≤200 to <300		71.4% (25)	28.6% (10)	
≤100 to <200		47.5% (19)	52.5% (21)	
>100		35.0% (7)	65.0% (13)	
MV duration, days	6 (4-10)	5 (3-8)	10 (7-16)	<.0001
MV after ICU	13.2%	9.6%	22.2%	0.031
ICU mortality	4.8%	1.5%	13.0%	0.003
ICU duration, days	7 (5-11)	6 (4-9)	11 (8-16)	<.0001

Acute Physiology and Chronic Health Evaluation II, APACHE II; body mass index, BMI; chronic kidney disease on hemodialysis, CKD on HD; continuous renal replacement therapy, CRRT; extracorporeal membrane oxygenation, ECMO; intensive care unit. ICU; INTELLiVENT-ASV®, I-ASV; mechanical ventilation, MV; PaO_2/F_IO_2 ratio, P/F ratio.

Table 2. Annuals trends associated with successful I-ASV

Year	2016	2017	2018
Number of included patients	N=29	N=68	N=92
I-ASV success, (n)	69.0% (20)	72.1% (49)	71.7% (66)
APACHE II	19 (17–26)	17 (14–25)	23 (18–27)
P/F ratio	281 (227–365)	288 (226–391)	260 (183–337)
Presence of infection	72.2%	75.0%	80.0%
CKD on HD	50.0%	66.7%	75.0%
Reasons for admission			
- Elective surgery	85.7%	94.1%	100.0%
- Emergent surgery	69.2%	75.0%	90.6%
- Medical reasons	55.6%	58.1%	54.0%
P/F ratio classification			
- Normal	82.4%	89.5%	92.3%
- Mild	50.0%	72.7%	75.0%
- Moderate	60.0%	37.5%	52.6%
- Severe	33.3%	33.3%	35.7%

Acute Physiology and Chronic Health Evaluation II, APACHE II; chronic kidney disease on hemodialysis, CKD on HD; INTELLiVENT-ASV®, I-ASV; PaO_2/F_IO_2 ratio, P/F ratio.

Table 3. Multivariate analysis for predicting successful ventilation with I-ASV

	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
	(Non-adjusted)		(adjusted)	
Age	0.99 (0.97–1.01)	0.550	1.01 (0.98–1.03)	0.663
Sex, male	1.43 (0.76–2.74)	0.268	1.39 (0.69–2.80)	0.356
BMI	0.99 (0.93–1.06)	0.798	0.99 (0.93–1.07)	0.986
Presence of sepsis	1.59 (0.84–3.07)	0.152	0.85 (0.40–1.83)	0.677
CKD on HD	1.62 (0.47–5.10)	0.426	1.04 (0.29–3.75)	0.957
P/F ratio	1.005 (1.002–1.008)	<.0001	1.003 (1.000–1.006)	0.051
APACHE II	0.91 (0.87–0.95)	<.0001	0.92 (0.87–0.96)	0.0006

Acute Physiology and Chronic Health Evaluation II, APACHE II; body mass index, BMI; confidential interval, CI; chronic kidney disease on hemodialysis, CKD on HD; INTELLiVENT-ASV®, I-ASV; PaO_2/F_IO_2 ratio, P/F

Figures

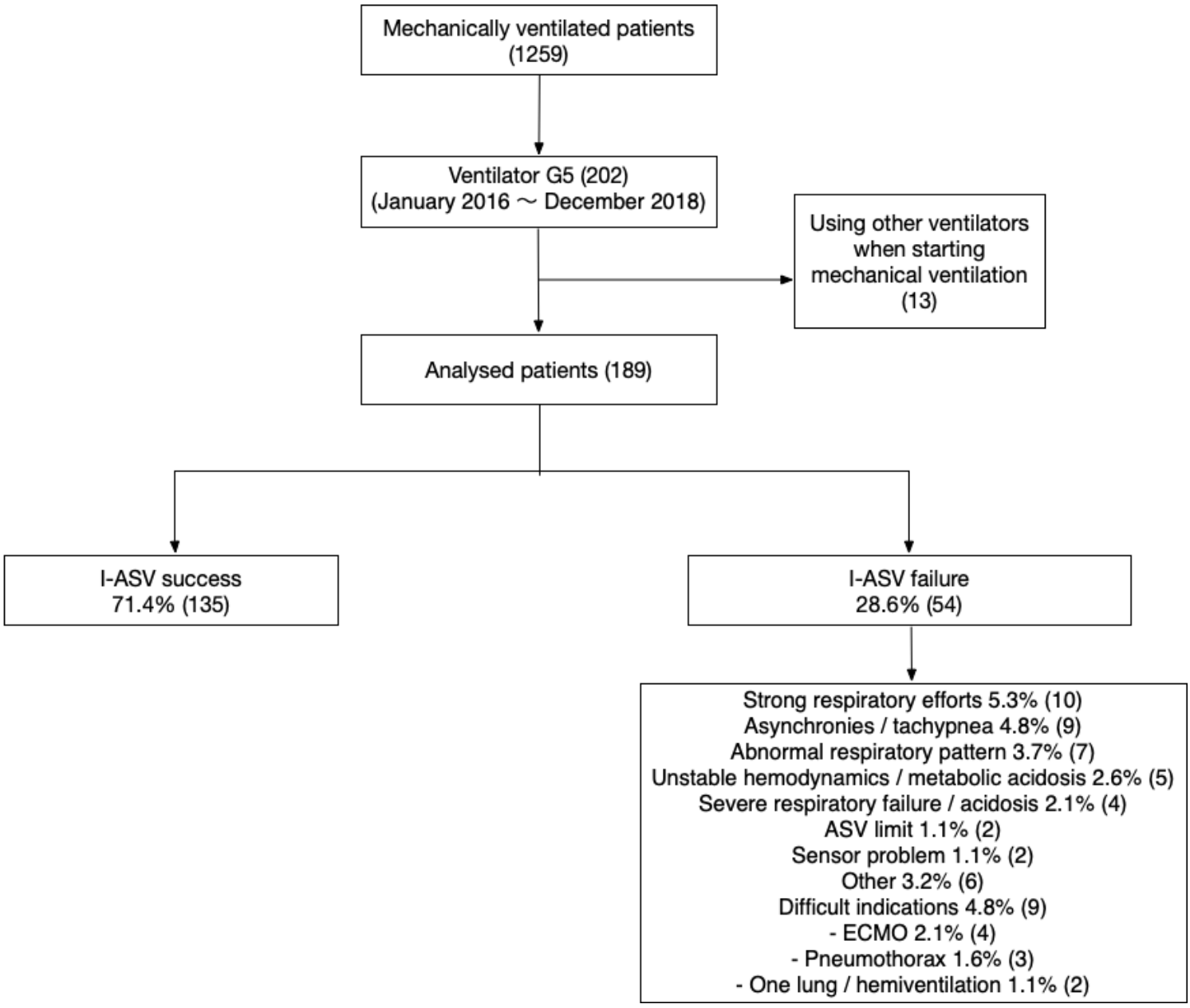

Figure 1

Flow chart showing the classification of the study patients.

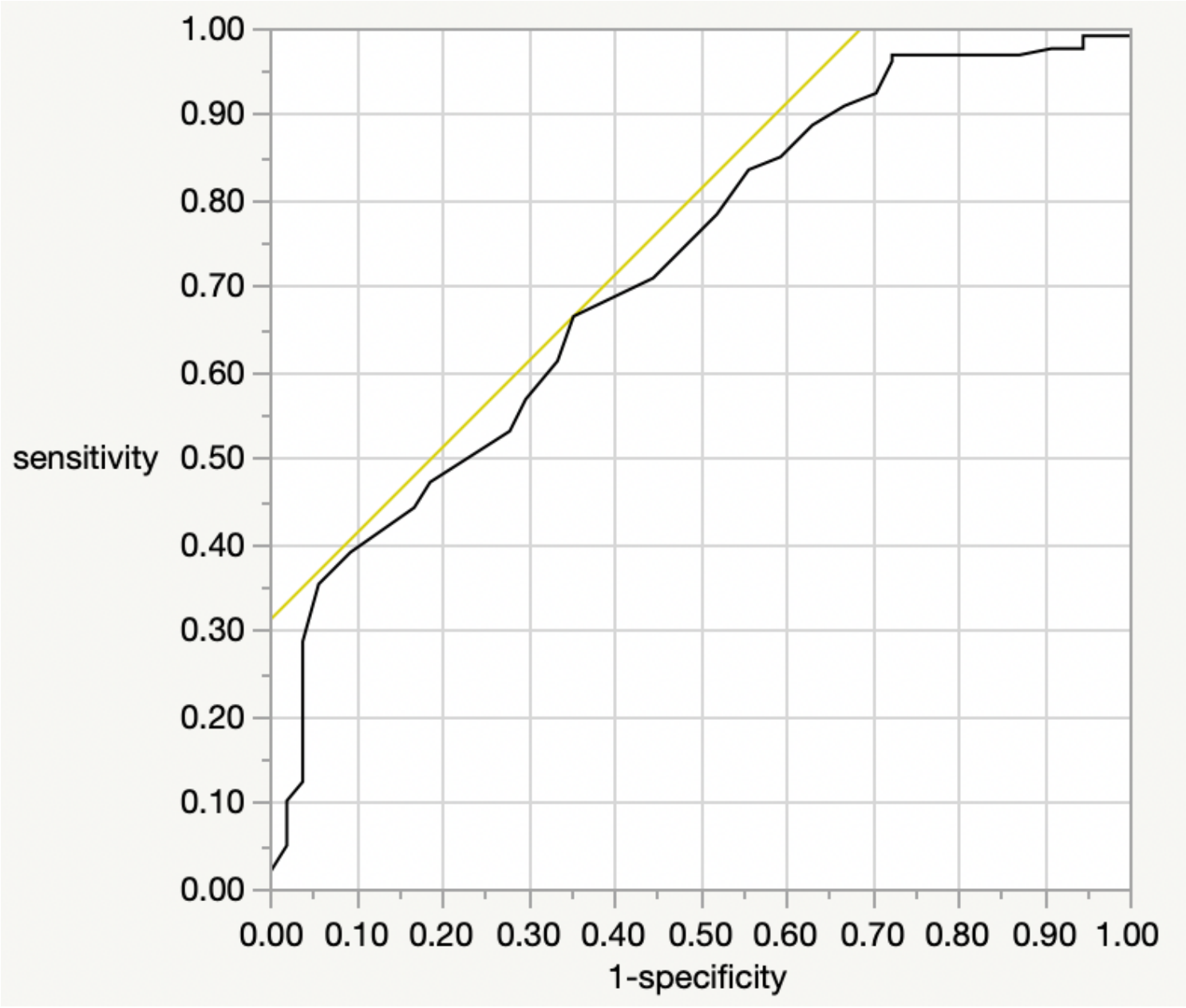

Figure 2

The area under the receiver operative curve compared with the APACHE II.