Secondary use of data extracted from a clinical information system to assess the adherence of tidal volume and its impact on outcomes.

Objectives

To extract data from Clinical Information Systems to automatically calculate high-resolution quality indicators to assess adherence to recommendations for low **tidal volume**.

Design

We devised two indicators: the percentage of time under mechanical ventilationwith excessive **tidal volume**(>8 mL/kg predicted body weight) and the percentage of patients who received appropriate **tidal volume** (≤8 mL/kg PBW) at least 80% of the time under **mechanical ventilation**. We developed an algorithm to automatically calculate these indicators from **Clinical Information System** data and analysed associations between them and patients' characteristics and outcomes.

Settings

This study has been carried out in our 30-bed polyvalent **intensive care unit** between January 1, 2014 and November 30, 2019.

Patients

All patients admitted to **intensive care unit**ventilated >72 hourswere included.

Intervention

Use data collected automatically from the **Clinical Information Systems** to assess adherence to **tidal volume** recommendations and its outcomes.

Main variables of interest

Duration of **mechanical ventilation**, **intensive care unit,ICU** length of stay and mortality.

Results

Of all admitted patients, 340 met the inclusion criteria. Median percentage of time under **mechanical ventilation** with excessive **tidal volume** was 70% (23%–93%); only 22.3% of patients received appropriate **tidal volume** at least 80% of the time. Receiving appropriate **tidal volume** was associated with shorter duration of **mechanical ventilation**and **intensive care unite** stay. Patients receiving appropriate **tidal volume** were mostly male, younger, taller, and less severely ill. Adjusted **intensive care unit** mortality did not differ according to percentage of time with excessive **tidal volume** or to receiving appropriate **tidal volume** at least 80% of the time.

Conclusions

Automatic calculation of process-of-care indicators from **Clinical Information Systems** high-resolution data can provide an accurate and continuous measure of adherence to recommendations. Adherence to **tidal volume** recommendations was associated with shorter duration of **mechanical ventilation** and **intensive care unit** stay.

Keywords: Mechanical Ventilation, Quality Indicators, Clinical Information System, Tidal Volume

Uso secundario de los datos del Sistema de Información Clínica para evaluar la adherencia a las guías de práctica clínica respecto al volumen tidal y su impacto en los resultados.

Objetivos

Extraer los datos del Sistema de Información Clínica para calcular automáticamente indicadores de calidad de alta resolución para evaluar la adherencia a las recomendaciones sobre el volumen tidal.

Diseño

Ideamos dos indicadores: el porcentaje de tiempo en **ventilación mecánica** con **volumen tidal** excesivo (>8 mL/kg peso ideal) y el porcentaje de pacientes con **volumen tidal** apropiado (≤8 mL/kg peso ideal) al menos el 80% del tiempo en **ventilación mecánica.** Desarrollamos un algoritmo para calcular automáticamente dichos indicadores con los datos de **sistema de información clínica** y analizamos su asociación con las características de los pacientes y su **evolución**.

Ambiente

El estudio se llevó a cabo en una **unidad de cuidados intensivos** polivalente de 30 camas desde el 1 Enero 2014 hasta el 20 Noviembre 2019.

Pacientes

Se incluyeron en el estudio todo los pacientes ingresados en la **unidad de cuidados intensivos** conectados a **ventilación mecánica**>72 horas.

Intervención

Usar los datos recogidos automáticamente desde el **sistema de información clínica** para evaluar la adherencia a las recomendaciones del **volumen tidal** y sus resultados.

Principales variables de interés

Días de **ventilación mecánica**, días de estancia en la **unidad de cuidados intensivos** y mortalidad.

Resultados

340 pacientes cumplieron los criterios de inclusión. El tiempo medio de**ventilación mecánica** con **volumen tidal** excesivo fue 70% (23%–93%); sólo el 22.3% de los pacientes recibió un **volumen tidal** apropiado al menos el 80% del tiempo. Recibir un **volumen tidal** apropiado se asoció con menos días de **ventilación mecánica** y de estancia en la **unidad de cuidados intensivos**. Los pacientes que recibieron un **volumen tidal** apropiado fueron más frecuentemente hombres, más jóvenes, más altos y menos graves. No hubo diferencias significativas en la mortalidad ajustada en relación con el porcentaje de tiempo de **volumen tidal** excesivo o recibir un **volumen tidal** apropiado al menos el 80% del tiempo.

Conclusiones

El cálculo automático de los indicadores de calidad desde el **sistema de información clínica** puede proporcionarnos una medida precisa y continua de la adherencia a las recomendaciones. La adherencia a las recomendaciones sobre el **volumen tidal** se asocia con menos días de **ventilación mecánica** y de estancia en la **unidad de cuidados intensivos**.

Palabras calve: Ventilación Mecánica, Indicadores de Calidad, Sistemas de información clínica, Volumen Tidal.

1. INTRODUCTION

A growing number of healthcare performance measures are being publicly reported. Patients, providers, payers and policymakers deserve valid, reliable and transparent quality measures[1]. Indicators are the best tools for measuring quality, but collecting the information needed to calculate them is time consuming and complex[2]. Information technology can provide**to**critical care with new tools to improve management, decision making and effectiveness of care[3].

Indicators should be measurable, reliable, valid and reproducible[4]. Using indicators based on data extracted from the **Clinical Information Systems (CIS)** can help ensure homogeneous definitions and reduce the time professionals need to invest in collecting data. Recently, our group showed that it is feasible to automatically generate the minimum dataset and **intensive care unit** (ICU) quality indicators with a data management tool we developed using business discovery techniques on an associative data model created from variables stored in the CIS[5].

Ventilator management is an essential part of critical care. However,**MV probably can aggravate acute lung injury as ventilator-induced lung injury (VILI), especially in patients with acute respiratory distress syndrome (ARDS)**[6]. As high **tidal volume (TV)** has been demonstrated to be prejudicial and produced volutrauma[7], the standard of care in these patients is protective mechanical ventilation with low **TV**(<8 ml/Kg **predicted body weight** (PBW))[8], reducing mortality by 22%[9]. Moreover, some studies conclude that **protective mechanical ventilation** is not only beneficial for patients with ARDS, but also improve outcomes in patients with healthy lungs[10,11]. A recent large epidemiologic study, LUNG SAFE, concluded that ARDS is underdiagnosed and often goes unrecognized until after significant delays[12]. Growing evidence supports the use of low **TV** as early as possible in patients with acute respiratory failure regardless of

whether ARDS has been diagnosed[10]. However, different studies show that patients with ARDS do not consistently receive low **TV** despite over 15 years' effort to ensure its adoption into clinical practice [13,14,15].

Our approach consists in taking profit of all the continuous measurements automatically collected by the CIS to create high-resolution quality indicators (HR-QI) to assess **TV,** improving snapshot-based assessments and saving time to healthcare professionals.

Our main objective was to define, implement and evaluate two HR-QI to assess adherence to clinical practice guidelines for **protective mechanical ventilation** in our ICU using data automatically collected in our CIS database. Our secondary objective was to analyze patients' characteristics according to those HR-QIand its impact on outcomes.

2. PATIENTS AND METHODS

2.1. Design

We included all non-coronary patients who received invasive MV in our 30-bed polyvalent ICU (xxx) between January 1, 2014 and November 30, 2019. We did not include coronary patients because they are attended by other specialists. We excluded patients whose height and/or weight was not recorded and those < 130 cm tall, for whom the PBW equation may not apply[16]. We also excluded patients who received MV<72 hours because they were not at risk for prolonged exposure to high **TV** and those ventilated with pressure support more than 20% of the time, because we were interested in **TV** delivery directly set by the physicians.

All patients or their legal representatives provided written informed consent. Our center's research ethics committee approved the study protocol (xxx).

2.2. Patient data capture

Since 2013, our ICU has been using a commercial CIS (Centricity Critical Care® from General Electric) to enter orders, document clinical acts, record medication administration and collect data. Moreover, mechanical ventilators are connected to the CIS, and all respiratory parameters are recorded every 2 minutes. All inputs are stored in a data storage repository. All data used in this study have been extracted from the CIS database by means of ETL (Extraction, Transform and Load) processes implemented with Python 3.

2.3. Clinical Variables

We extracted the following variables: age, sex, admission source, reason for admission **(classification according to variables of the Minimum Data Set of Intensive Care Unit CMBD-UCI of the**Sociedad Española de Medicina Intensiva y Unidades Coronarias (SEMICYUC) criteria[5]) (**Supplementary Table 1**), patient type (medical or surgical), admission type (urgent or scheduled), height, weight, APACHE II and the worst values of clinical variables as mean arterial pressure, body temperature, heart rate, pulse oximetry (SpO_2), pH, $PaCO_2$, serum lactate, serum bicarbonate, Richmond Agitation Sedation Scale (RASS), Sequential Organ Failure Assessment (SOFA) score, administration of vasopressor drugs, continuous renal replacement therapy (CRRT) and administration of analgesics and sedatives in the first 48 hours of MV.

2.4. Ventilatory variables

We analyzed the set and/or observed values of the following ventilatory variables: **TV**, positive end-expiratory pressure (PEEP), peak pressure (Ppeak), plateau pressure (Pplat), respiratory rate (RR) and fraction of inspired oxygen (FiO_2). All ventilation variables were extracted as median values for each hour during the first 48 hours after starting MV (**Table 1**). **For calculate HR-QI we have recorded TV during the entire time in MV**.

Because PaO_2 was not recorded in all patients, instead of PaO_2/FiO_2 we used pulse oximetry (SpO_2)/ FIO_2 [S/F] ratio, which correlates acceptably with PaO_2/FiO_2[17].

2.5. Primary endpoints

We designed two HR-QI to perform a high-resolution assessment of the adherence to low **TV** recommendations defined as follows:

1) *Percentage of time on MV with excessive **TV** (%t**TV**ot),* defined as the time under MV in which the **TV** is above the recommended values [> 8 mL/kg PBW] and calculated according to the formula:

$$\frac{\text{TimeonMVwithTV} > \frac{8\text{ml}}{\text{KgPBW}}}{\text{TotaltimeonMV}} \text{ x } 100$$

2) *Percentage of patients who received appropriate **TV** (%p**TV**a),* calculated according to the formula:

$$\frac{\text{N°ofpatientswithTV} \leq \frac{8\text{ml}}{\text{KgPBW}} \text{ during} > 80\% \text{timeonMV}}{\text{N°ofpatientsonMV}} \text{ x } 100$$

PBW was calculated according to the formulas:

$$\text{Men: } 50 + [0.91 \text{ x } (\text{Heightincm} - 152.4)]$$
$$\text{Women: } 45.5 + [0.91 \text{ x } (\text{Heightincm} - 152.4)]$$

2.6. Secondary endpoints

Duration of invasive MV, defined as the number of days between the date of intubation and the date of **MV** disconnection (**picked by a nurse the first day of MV disconnection into the CIS**) or death; ICU length of stay (LOS), defined as the number of days between the date of admission to the ICU and the date of discharge from the ICU; hospital LOS, defined as the number of days between the date of admission to the hospital and the date of discharge from the hospital; and ICU and hospital mortality.

2.7. Statistical Analysis

Categorical variables are expressed as counts (percentage) and continuous variables as medians (interquartile range). To compare patient demographic and clinical characteristics between two groups, we used the chi-square test or Fisher's exact test for categorical variables, as appropriate, and Student's t-test or the Mann–Whitney U test for continuous variables. For univariate comparisons with more than two groups, we used the chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables. Multivariate comparisons were performed using binary logistic regression and models were evaluated using its accuracy and area under the receiver operating characteristic curve (AUC). Logistic regression coefficients were converted to odds ratios to easy interpretability of covariates influence in each group.

To avoid spurious significance between variables related to the large volume of data analyzed, we set significance at $p < 0.005$[18].

To characterize patients' profile according to our first HR-QI *%t**TV**ot*, patients were categorized into quartiles. To investigate the association between baseline variables (at ICU admission and first 48 h of invasive MV) and *%t**TV**ot*, we first performed univariate analysis. Afterwards, we used binary logistic regression to compare the fourth (high-

est) quartile against the combined group of patients in the first, second and third quartiles in a multivariate model including only demographics and severity covariates that were significant in the univariate analysis.

To characterize patients' profile according to our second HR-QI %*pTVa*, patients were divided in two groups, those who accomplished the HR-QI and those who do not. To investigate the association between baseline variables and the two groups, we first performed univariate analysis. Afterwards, we used binary logistic regression to compare them in a multivariate model including only demographics and severity covariates that were significant in the univariate analysis.

To evaluate the association between inappropriate ventilation (according to our two HR-QI) and mortality, we used univariate and binary logistic regression analysis following the same procedure but including both HR-QI in the final analysis. Analyses were done with Python (Python Software Foundation - Python.org) and R (CRAN-R project) software.

3. RESULTS

3.1. Population characteristics

We analyzed data from 340 patients (**Figure 1**) whose median age was**58.4** (48.8–71.0) years; 235 (69%) were men with median APACHE II score of 24 **(19-30)**points and median SOFA score of 8 **(6-10)**points (**Table 1**).

3.2. HR-QI (%tTVot)

The results of our first HR-QI showed a median *%tTVot* of 70% (23% – 93%), with a median excessive volume of 8% (3%-15%) over the amount required according to patient's PBW. Regarding to patient's characterization according to our first HR-QI, patients in the first quartile included a greater proportion of men and were younger, taller,

and less severely ill (p<0.001) in comparison with the rest of quartiles. Comparing the first against the fourth quartile, the median excessive volume over the one required according to their PBW was lower [4% vs. 17%, respectively, p<0.001). It is important to highlight that no differences were found in the set absolute **TV**amount (mL) between the extreme quartiles (p=0.06), suggesting that the relative amount to PBW (and therefore the height) is what makes the big difference (p=0.001 and p<0.001 for set and measured **TV** relative to PWB respectively). No other differences were observed in respiratory or MV variables. Even if ICU LOS, duration of MV and ICU and hospital mortality were higher in the fourth quartile than in the first, those differences were not significant. **(Figure 2 and Supplementary Table 2).**

In the multivariate analysis, only height was independently associated with *%t**TV**ot* **(Figure 2)**. We obtained an accuracy of 77.94%and an AUC curve of **0.81(0.74-0.86)(Supplementary Figure 1).**

3.3. Second HR-QI (%pTVa*)*

Of the 340 patients analyzed, only 76 (22.3%) received appropriate **TV**according to the definitions of our second HR-QI. Patients receiving appropriate **TV** were younger and taller, with a greater predominance of men and lower severity of illness. As expected, *%t***TV***ot* and excessive volume were higher in the group receiving inappropriate **TV**. Although set **TV** did not differ between groups, measured **TV** adjusted for PBW was higher in the group receiving inappropriate **TV (Figure 3)**. Duration of MV and ICU LOS were significatively shorter in the group receiving appropriate **TV (p<0.05) (Figure 4 and 5)**. No differences in ICU mortality were observed between the groups (**Figure 3 and Supplementary Table 3**).

In the multivariate analysis, only height was associated with having an adequate **TV**. **(Figure 3)**. We obtained an accuracy of 80.59%and an AUC curve of **0.82(0.76-0.87)(Supplementary Figure 2).**

3.4. Variables independently associated with ICU mortality

The crude mortality rate was 44.4% in the ICU and 45.9% in the hospital **(Table 1)**. Patients who died were older**(73.5 vs. 62.9)**, with higher APACHE II score**(25 vs. 22)**, higher lactate concentration **(2.3 vs 1.9)**and lower SpO2 level**(95 vs. 96)(Supplementary Table 4)**.

We included all these 4 significant variables resulted from the univariate analysis together with our HR-QI target variables: *%t**TV**ot* and ***TV**a*. We found that only age was independently associated with mortality (**Supplementary Figure 3**). We obtained an accuracy of 67.94% and an AUC curve of 0.74 **(0.68-0.8) (Supplementary Figure 4).**

4. DISCUSSION

Technological advances since the first CIS and patient data management systems, which were introduced in the late 1980s [19], have enabled the integration of a wide range of bedside devices and automatic data collection[20]. To date, systematic reviews on using CIS have concentrated primarily on their organizational impact (e.g. charting, documenting, patient care, etc.) rather than their impact on clinical outcomes and quality assessment[21,22].

Our results support the view that the secondary use of data from the CIS can be very useful to assess adherence to clinical practice guidelines [23,24]and create more accurate quality indicators, helping us to improve the process of care in our ICU. We adapted current definitions of indicators to allow them to be automatically calculated with data from our CIS[25].

We have been able to perform a high-resolution evaluation of the adherence to recommendations for low **TV** in MV using data automatically and continuously collected (one measurement each 2 minutes) into the CIS. Since MV is dynamic and changeable 24 hours a day, data extracted in other studies where respiratory variables have been measured once or twice a day[10,12,13], provide an incomplete picture of compliance with recommendations for **protective mechanical ventilation**.**Our group have also carried out different studies analyzing the efficiency of random safety analysis on structure, process and outcome indicators, including protective mechanical ventilation, without detecting such a great lack of adherence as the CIS [26,27]. Probably both methodologies are complementary.**

Despite several studies reported benefits of low **TV** and it is recommended in clinical practice guidelines, there is poor adherence to them[13,14,15]. We found that, on average, our patients received **TV** above the recommended cutoff (8 mL/kg PBW) 70% of time they were under MV. These results are in line with those reported in other studies[28]. Among various possible explanations for these findings, one that stands out is the use of actual body weight instead of PBW to set **TV**. Using PBW seeks to minimize volutrauma by better estimating the patient's lung capacity; lung capacity and respiratory system compliance relate more closely to height than to weight[16]. We suspect that the main reason for not following guidelines on lower **TV** in our series was inaccurate calculation of PBW. In fact, we have observed that shorter patients and women (generally shorter than men) were more common ventilated with higher **TV**, as found in other studies [12,14,29,30]. In a secondary analysis of data from the LUNG SAFE study, McNicholas et al.[31] recently demonstrated important sex differences in the management and outcomes of patients with ARDS; lower **TV** was applied in only half the female patients,

and shorter women more likely to receive higher **TV** than shorter men. Moreover, mortality rates were significantly higher in women.

We observed that the duration of MV and ICU LOS were higher in patients with higher percentage of time on MV with **TV** above the target level and in those patients who received **TV** above the target level for more than 80% of the time, correlating with previous literature [28]. We found no association between the proportion of time with high **TV** and mortality. These findings are likely due to other factors that can impact mortality; for example, Serpa Neto et al demonstrated that, even at low **TV** and low driving pressure, high mechanical power is associated with worse outcomes[32].**Although our study have been focused on TV, CIS can also calculate driving pressure and mechanical power values in a continuous way, that would be studied in the future.**

It is widely recognized that **protective mechanical ventilation**with lower **TV** is associated with better clinical outcomes in patients with ARDS[9]. Although most studies have shown that high **TV** is associated with increased complications also in patients with healthy lungs[10,11], evidence supporting **protective mechanical ventilation**in patients without ARDS is inconclusive[33]. However, there are good reasons to strongly consider using low **TV** in all patients[13], even at the initiation of MV[28]. Lung damage can occur within hours of initiating MV with inappropriate settings, ARDS is often unrecognized until after a delayed onset inflammatory process and critically ill patients are at risk of other causes of lung injury. Therefore, in addition to a therapeutic modality, low **TV** can be useful as a preventive measure, especially in patients with conditions involving increased risk of lung injury, such as sepsis, trauma, or high-risk surgeries[34].

Quality indicators proposed for respiratory care and MV did not include **protective mechanical ventilation**[35,36]. However, considering findings of higher mortality in ARDS patients ventilated with high **TV** in the last decade[9,12], more recent quality-control

guidelines from various countries include indicators related to **protective mechanical ventilation**[37,38], although some refer only to indicators of structure, for example the availability of a written protocol or routine for a lung-protective ventilatory strategy[39]. One reason why indicators that could provide better information about MV processes are not implemented is that accurate information to measure them is unavailable or difficult to obtain. Our study shows that this problem can be overcome.

Our study has important limitations that must be pointed out. First, our analysis included only patients who received volume-controlled MV. We did not analyze patients receiving pressure-controlled or pressure-support ventilation, because in this context **TV** is influenced by the applied airway pressures as well as the compliance of the respiratory system[40], increasing the margin of error in determining actual **TV** set or in analyzing its impact on outcomes. Second, we did not consider the characteristics of MV in the emergency room or operating room prior to ICU admission, which may affect outcomes[41]; however, including only patients undergoing > 72 hours MV in the ICU probably reduced the impact of ventilation outside the ICU on outcomes drastically. Furthermore, because we were unable to calculate PaO_2/FiO_2 in all patients, we used SaO_2/FiO_2 instead; SaO_2/FiO_2 is accessible and reliable, can be obtained continuously, and correlates acceptably with PaO_2/FiO_2 [17]. Nevertheless, our study has the strength of using continuous data from a very homogeneous population of ventilated patients. Data-based decision making depends on the quality of the data and we have taken steps to guarantee their quality. An earlier study demonstrated that none of the variables collected by our data management tool differed significantly from those collected manually by trained staff [5].

5. CONCLUSION

There is low adherence to clinical practice guidelines related to **protective mechanical ventilation.** The amount **TV** over target time and the amount of excessive **TV** worsen patients' outcomes. Men, taller, younger, and less severely ill are better ventilated according to clinical practice guidelines, which suggest that PBW needs to be calculated more carefully in our unit. Data extracted from the CIS can provide invaluable information about deviations from recommended clinical practice. Automatically generating HR-QI allowed us to identify actions to improve the quality of care in our ICU, sparing professionals the tedious, time-consuming tasks of collecting data and calculating indicators.

List of abbreviations

Clinical information system (CIS); Intensive care unit (ICU); Predicted body weight (PBW); Acute respiratory distress syndrome (ARDS); Tidal volume (**TV**); Mechanical ventilation (MV); Extraction Transform and Load (ETL); Spanish Intensive Care Society - *Sociedad Española de Medicina Intensiva y Crítica y Unidades Coronarias* (SEMICYUC); Acute Physiology And Chronic Health Evaluation II (APACHE II); Pulse oximetry (SpO_2); Richmond Agitation Sedation Scale (RASS); Sequential Organ Failure Assessment (SOFA); Renal replacement therapy (CRRT); End-expiratory pressure (PEEP); Peak pressure (Ppeak); Plateau pressure (Pplat); Respiratory rate (RR); Fraction of inspired oxygen (FiO_2); Length of stay (LOS).

Authors' contributions

Conceptualization: XXX, XXX, XXX

Data curation; Formal analysis; Software: XXX, XXX

Funding acquisition: XXX

Methodology: XXX, XXX

Supervision: XXX, XXX

Validation: XXX

Writing - original draft: XXX, XXX, XXX, XXX

Writing - review & editin: XXX, XXX, XXX

Conflict of interest

This study was supported by grants from the **XXX** and **XXX**. The authors declare they have no competing interests.

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UCI Data-Analitics: XXX, XXX, XXX, XXX.

XXX edited the manuscript.

Clinical Relevance Statement

Our study demonstrates how the data stored into the Electronic Health Records through the Clinical Information Systems can be exploited to build high-resolution quality indicators (HR-QI) of care without any extra efforts for the healthcare professionals. We evaluated two HR-QI to assess tidal volume and its impact on outcomes.

Protection of Human and Animal Subjects

The study was performed in compliance with the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects and was approved by the Ethics and Clinical Research Committee (XXX).

Consent to participate

All patients or their legal representatives provided written informed consent**.**

Consent for publication

Our manuscript doesn't contain any individual person's data

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Code availability

The code for the current study is available from the corresponding author on reasonable request.

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Table 1: Characteristics of patients included in the study (n=340)

Variables	**Values**
Demographics (at admission)	
Age**(years), median (p25-75)**	**58.4**(48.8-71.0)
Male**sex, n (%)**	234 (68.8)
Weight**(kg)**, **median (p25-75)**	75.0 (70-85.0)
Height **(cm)**, **median (p25-75)**	170 (165-175)
Admission type Medical admission, n (%) Emergency surgical admission, n (%) Elective surgical admission, n (%)	 220 (64.7) 112 (32.9) 8 (2.4)
Reason for admission Respiratory failure, n (%) Sepsis, n (%) Others, n (%)	 82 (24.1) 51 (15) 207 (60.9)
Severity scores (at 24 hours of admission)	
APACHE [a] II score**(points)**, **median (p25-75)**	24 (19-30)
SOFA [b] score **(points)**, **median (p25-75)**	8 (6-10)
Respiratory and mechanical ventilation (First 48h)	
SpO_2 [c]**(%)**	96 (94-98)
SpO_2/ FIO_2, **median (p25-75)**	240 (160-312.9)
SpO_2/ FIO_2, n(%)	**259 (76.2)**
FiO_2 [d]**(%)**	35 (30-45)
% controlled MV modes	93 (86-99)
Set MV [e] flow (L/min), **median (p25-75)**	60 (50-60)
Positive end-expiratory pressure **(cmH2O), median (p25-75)**	5 (5-8)
Peak pressure**(cmH2O), median (p25-75)**	24 (22-28)

Plateau pressure**(cmH2O), median (p25-75)**	20 (17-25)
Observed respiratory rate (breaths/min), **median (p25-75)**	17 (16-19)
Set respiratory rate (breaths/min), **median (p25-75)**	18 (16-20)
Set tidal volume (mL), **median (p25-75)**	520 (480-552)
Observed tidal volume (mL), **median (p25-75)**	520 (480-560)
Set tidal volume (mL/predicted body weight), **median (p25-75)**	6.8 (6.0-7.6)
Observed tidal volume (mL/predicted body weight), **median (p25-75)**	6.8 (5.9-7.5)
Clinical and laboratory variables (first 48 hours)	
Heart rate (beats per minute), **median (p25-75)**	102 (87-118)
Mean arterial pressure (mmHg), **median (p25-75)**	68 (63-72)
Serum lactate (mmol/L), **median (p25-75)**	2.1 (1.5-3.0)
Body temperature**(ºC)**, **median (p25-75)**	37 (36.5-37.5)
Richmond Agitation-Sedation Scale **(points)**, **median (p25-75)**	-3 (-3 to -2)
Treatments and outcome (first 48 hours)	
Vasoactive drugs, **n (%)**	243 (71.5)
Sedative drugs, **n (%)**	318 (93.5)
Neuromuscular blocking agents, **n (%)**	47 (13.83)
Continuous renal replacement, **n (%)**	42 (12.4)
Died in ICU, **n (%)**	151 (44.4)
Died in hospital, **n (%)**	156 (45.9)

(a) APACHE: Acute Physiology And Chronic Health Evaluation, (b) SOFA: Sequential Organ Failure Assessment, (c) SpO2: oxygen saturation from pulse oximetry, (d) FiO2: fraction of inspired oxygen, (e) MV: mechanical ventilation. Data are shown as median (interquartile range) or number (percentage) of patients, as appropriate.

Figure 1: Flow chart of patients included in the study.

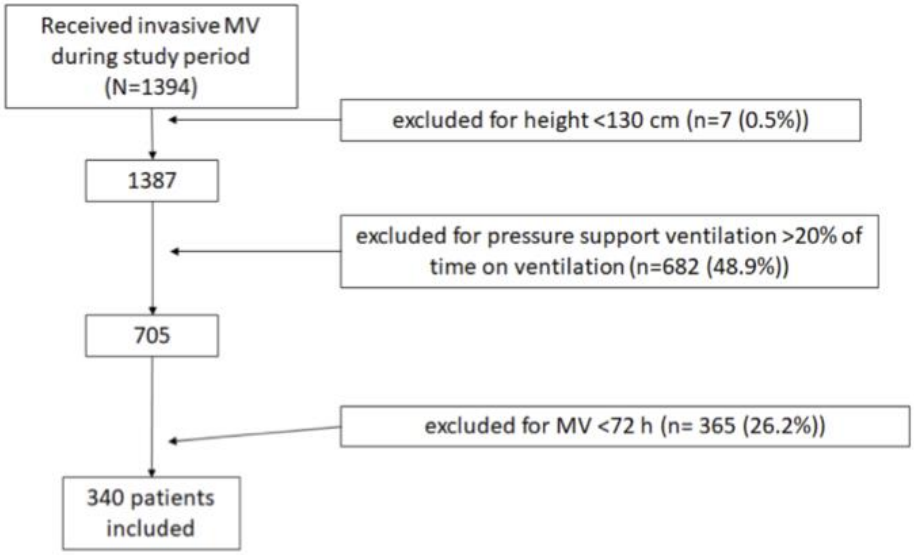
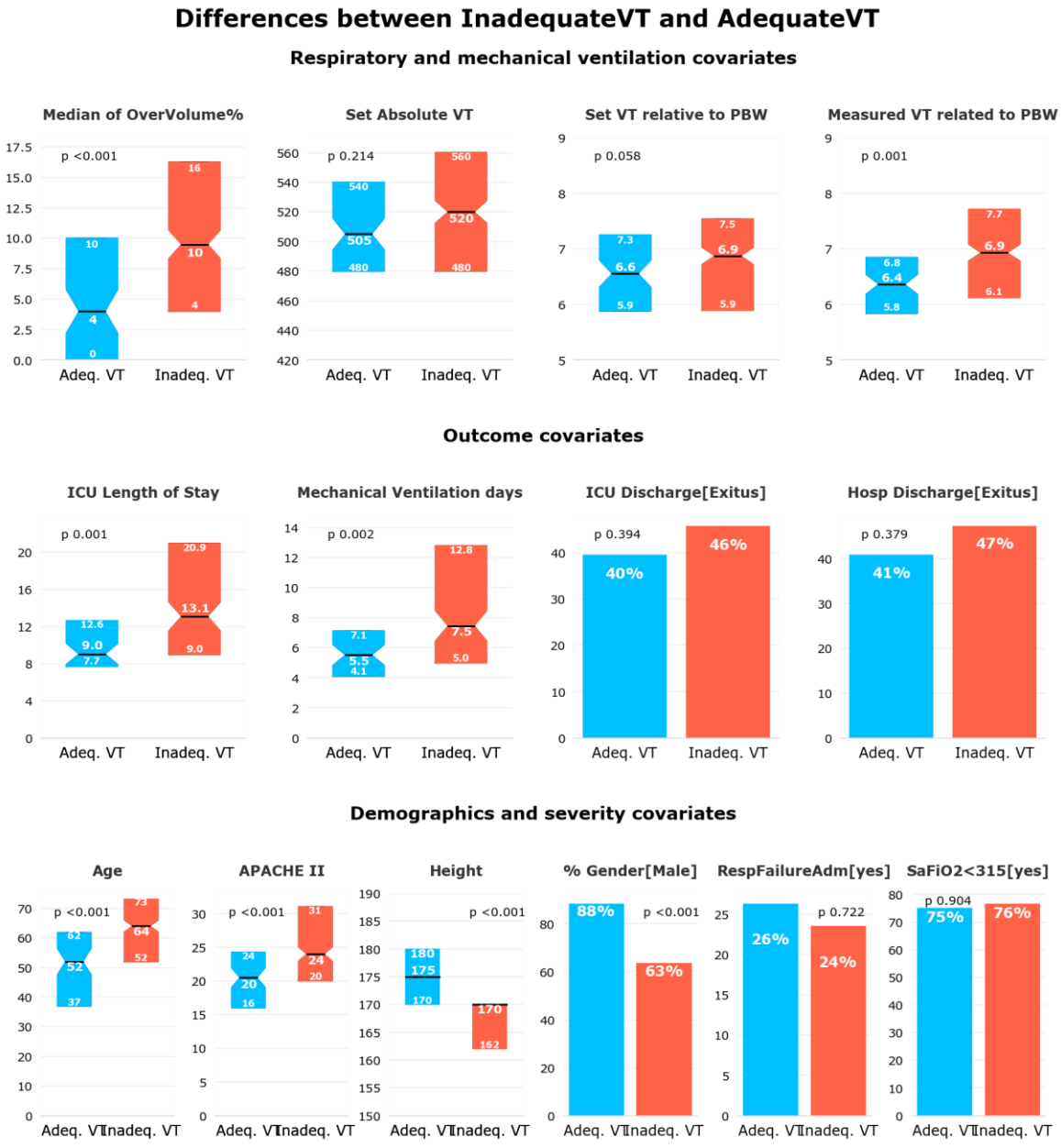
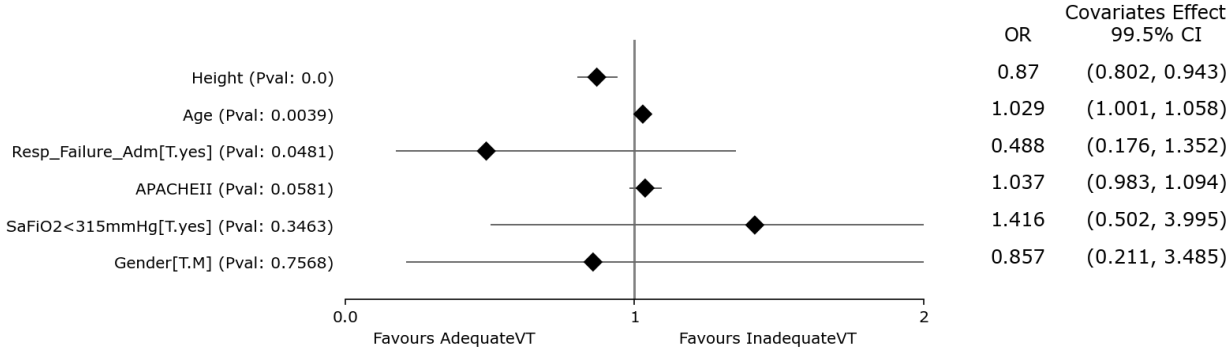


Figure 2: Univariate and multivariate differences for HR-Q1 (%tVot)

- In the univariate analysis, patients in Q4 (**highest** %t***TV***ot) have higher set and measured **TV** relative to PBW, but not in absolute **TV**. There is no significant difference between Q1 and Q4 in outcome covariates. **There is no difference in the distribution of patients with SaFiO2<315 or admitted for respiratory failure in the quartiles**. Patients in Q1 were mostly male, younger, taller, and less severely ill. (Significance at $p < 0.005$).
- In the multivariate analysis, **height was the most associated variable** with *%t*TV*ot*. (Significance at $p < 0.005$).

Figure 3: Univariate and multivariate differences for HR-Q2 (%pTVa)





	Covariates Effect
OR	99.5% CI
0.87	(0.802, 0.943)
1.029	(1.001, 1.058)
0.488	(0.176, 1.352)
1.037	(0.983, 1.094)
1.416	(0.502, 3.995)
0.857	(0.211, 3.485)

- In the univariate analysis, patients receiving appropriate **TV** (**TV**a) have shorter **ICU** length of stay in and less mechanical ventilation days. **There is no difference in the distribution of patients with SaFiO2<315 or admitted for respiratory failure in the quartiles.** Patients receiving **TV**a were mostly male younger, taller, and less severely ill. (*S*ignificance at $p < 0.005$).
- In the multivariate analysis, only height was independently associated with having an adequate **TV**. (*S*ignificance at $p < 0.005$).

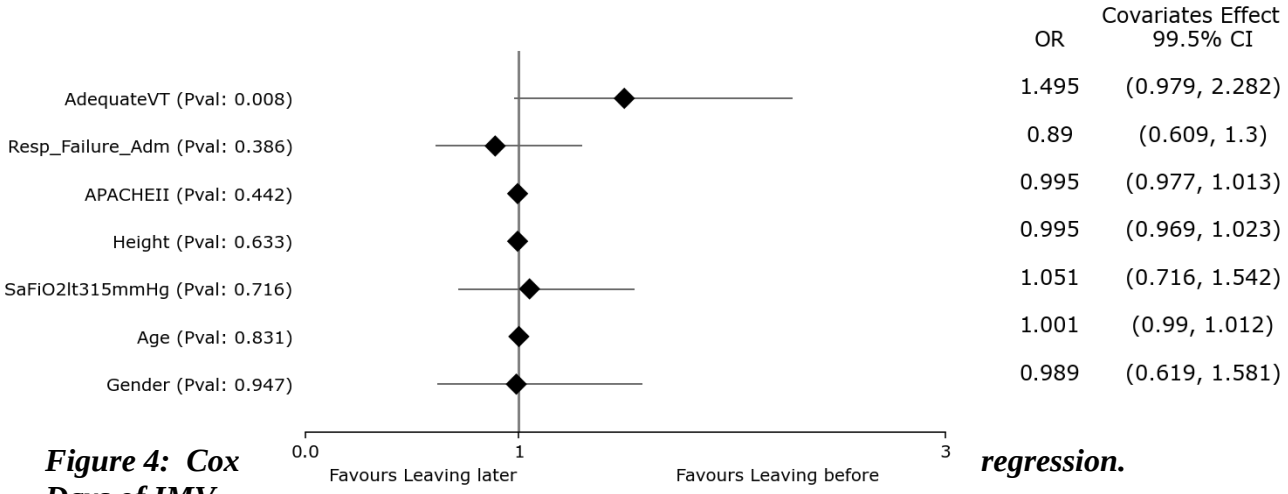
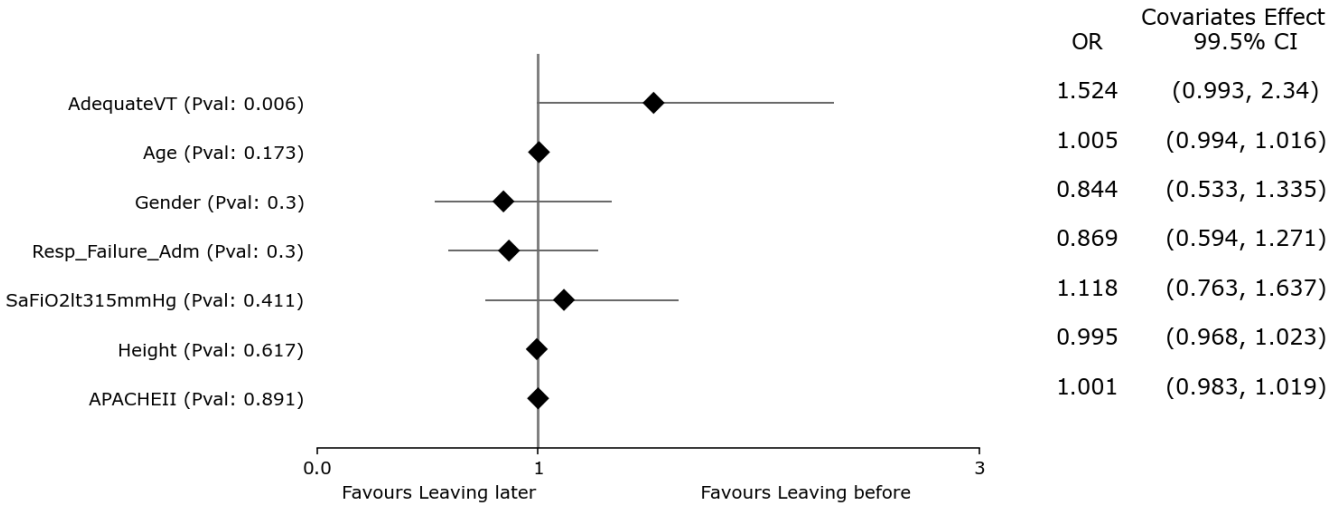


Figure 4: Cox regression. Days of IMV.

- Adequate VT is the unique variable with $p<0.05$. Adequate VT is the most related variable with the number of days in mechanical ventilation.

Figure 5: Cox regression. ICU length of stay.



- Adequate VT is the unique variable with $p<0.05$. Adequate VT is the most related variable with ICU length of stay.