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TITTLE: "Community acquired pneumonia: Risk factors associated with mortality in Ecuador – A retrospective cohort study"

Trabajo de integración curricular presentado como requisito para la obtención del título de Ingeniero Biomédico

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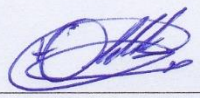

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Dedication

This thesis is dedicated with great affection towards my parents, Ana Gabriela and Pio Ernesto, who have given me their strength, wisdom, and support since the first day that I chose to be part of Yachay Tech. If it was not for the bases of their education, I could not be the person I am today. In the same way, I dedicate my achievements to my sister Fátima Sofía and my grandparents Ana María and Rosalino. They were constant support from my childhood until the course of each stage of my academic training.

Otto Fernando Proaño Arboleda

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El presente trabajo está dedicado con mucho cariño hacia mis padres, Ana Gabriela y Pio Ernesto quienes me han brindado su fortaleza, sabiduría y apoyo desde el primer día en que elegí ser parte de la Universidad Yachay Tech. De no ser por los cimientos de su educación no podría ser la persona que soy a día de hoy. De igual manera dedico mis logros hacia mi hermana Fátima Sofía y mis abuelos Ana María y Rosalino quienes fueron un soporte constante desde mi niñez hasta el transcurso de cada etapa de mi formación académica.

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Otto Fernando Proaño Arboleda

Reconocimiento

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Otto Fernando Proaño Arboleda

Abstract

Community-acquired pneumonia (CAP) remains one of the most relevant diseases associated with mortality in Ecuador. This study aims to determine what factors are associated with CAP mortality in Ecuadorian adults. Risk scales PS-Index and CURB-65 scores are used to classify the risk of dying from CAP. However, external factors can improve their effectiveness in certain populations. A retrospective cohort study was carried out in patients older than 21 years with CAP's primary diagnosis from the Hospital del IESS Quito Sur in November and December 2018. Simple logistic regression (SLR), and multiple logistic regression (MLR) analyzes were performed using the IBM SPSS Statistics 25 software. A total of 84 patients were hospitalized for CAP, of which 19 (22.6%) died. Variables that are significantly associated with the risk of dying from CAP were age (OR: 1,067; 95% CI: 1,008-1,129; $P = 0.026$) and mental disorders (OR: 8,060; 95% CI: 1,194-54,384; $P = 0.032$). Age is considered an essential factor in both scores and mental disorders only in PS-Index. Therefore, no factors external to the scores were found that could improve their prediction. In conclusion, age and mental disorders are significant predictors of mortality in patients with CAP.

Keywords: Community-acquired pneumonia; Pneumonia Severity Index score; CURB-65 score; Risk factor; mortality.

Resumen

La neumonía adquirida en la comunidad (NAC) sigue siendo una de las enfermedades más relevantes asociadas a la mortalidad en Ecuador. Este estudio tiene como objetivo determinar qué factores están asociados con la mortalidad por NAC en adultos ecuatorianos. Las escalas de riesgo PS-Index y las puntuaciones CURB-65 se utilizan para clasificar el riesgo de morir por NAC. Sin embargo, los factores externos pueden mejorar su eficacia en determinadas poblaciones. Se realizó un estudio de cohorte retrospectivo en pacientes mayores de 21 años con diagnóstico principal de NAC del Hospital del IESS Quito Sur en noviembre y diciembre de 2018. Análisis de regresión logística simple (SLR) y regresión logística múltiple (MLR) fueron realizados mediante el software IBM SPSS Statistics 25. Un total de 84 pacientes fueron hospitalizados por NAC, de los cuales 19 (22,6%) fallecieron. Las variables que se asociaron significativamente con el riesgo de morir por NAC fueron la edad (OR: 1.067; IC del 95%: 1.008-1.129; P = 0,026) y las enfermedades mentales (OR: 8.060; IC del 95%: 1.194-54.384; P = 0,032). La edad se considera un factor esencial en las dos escalas de riesgo y los trastornos mentales solo en el índice PS-Index. Por tanto, no se encontraron factores externos a las puntuaciones que pudieran mejorar su predicción. En conclusión, la edad y la enfermedad mental son predictores de mortalidad extremadamente importantes en pacientes con NAC.

Palabras clave: Neumonía adquirida en la comunidad; Puntuación del índice de gravedad de la neumonía; Puntuación CURB-65; Factor de riesgo; mortalidad.

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INTRODUCTION AND JUSTIFICATION

Community-acquired pneumonia (CAP) is a type of lung infection characterized by contracted in the community rather than in hospital. It is determined by clinical common symptoms and signs such as cough, sputum production, pleuritic chest pain, fever, tachypnoea, and rales with a respective radiological confirmation. CAP is a common disorder which is potentially life-threatening, especially in patients with associated risk factors (Loeb, 2010; Poetter-Lang & Herold, 2017). Several studies have shown that the incidence of CAP is around 10 cases per 1000 habitants per year, of which a considerable percentage are subject to death (Irizar Aramburu et al., 2013; Jokinen et al., 1993; Marrie, 2014). In 2019, according to the National Institute of Statistics and Censuses of Ecuador (INEC), influenza and pneumonia were the 4th cause of mortality in the population, are responsible for 4,096 (5.6% of total) deaths in the country (Instituto Nacional de Estadística y Censos INEC, 2019).

In general, there exist two evident risk populations that have been identified throughout the years. The first in children younger than <5 years and adults older than ≥ 65 (Almirall, Serra-Prat, Bolíbar, & Balasso, 2017; Cardinale, Rita, Felicia, Pignatelli, & Esposito, 2013; Fujiki, Kawayama, Ueyama, Ichiki, & Aizawa, 2007; L. Liu et al., 2015). The World Health Organization (WHO) places pneumonia as the leading cause of infant mortality globally, although it is estimated that the vast majority of cases in the world (over 95%) take place in developing countries (Rudan, Boschi-Pinto, Biloglav, Mulholland, & Campbell, 2008). However, older adults are also susceptible to pneumonia and more likely to die from this infection than younger populations. Depending on the symptoms older patients with pneumonia that require hospitalization have more risk to develop complications during the recovery process (Fein & Niederman, 1994).

It should be noted that CAP can be caused by various microorganisms, including bacteria, viruses, and fungi. Dozens of microorganisms have been identified as possible etiological agents, the most common being *Streptococcus pneumoniae*, *Haemophilus influenzae, Chlamydia pneumoniae* ,and *Mycoplasma pneumoniae*. (Almirall, Serra-Prat, & Bolibar, 2016; Lim et al., 2001; Micek, Kollef, Reichley, Roubinian, & Kollef, 2007). Studies have suggested that some lifestyle factors such as smoking and alcoholism, as well as the presence of comorbid conditions such as chronic respiratory, cardiovascular diseases,

cerebrovascular disease, immunosuppressive therapy, cancer, diabetes, dementia, HIV, are important risk factors (Almirall et al., 2016, 2017; Fujiki et al., 2007; Torres, Peetermans, Viegi, & Blasi, 2013). Systems for risk assessment of patients with CAP have currently been developed. Such is the case of the evaluations of British Thoracic Society forecast index called CURB-65 (Confusion, Urea nitrogen, Respiratory rate, Blood pressure, 65 years of age and older) and CRB-65 score; the latter does not include uric nitrogen (Aujesky et al., 2005; Dwyer, Hedlund, Henriques-Normark, & Kalin, 2014; Ebell, 2006; Lim et al., 2003). The so-called Pneumonia Severity Index (PSI) that has a higher degree of effectiveness is commonly used. The advantage of using the PSI score is that having more variables ranging from vital signs, demographics, clinical and sociodemographic variables, it achieves a higher degree of specificity and sensitivity when assigning a risk estimate (Aujesky et al., 2005; Fine et al., 1997).

Although several studies indeed endorse the different scores for pneumonia severity index with similar results, there are also small factors that vary depending on the country and even the hospital or entity in which these studies are carried out. These differences can be noticed in observational studies between different countries (Almirall et al., 2017; Torres et al., 2013). The lack of studies in Ecuador that document the variables associated with mortality from CAP means that the protocols to be followed for cases of CAP are based on information from other countries such as the US, UK or Spain, which have different lifestyles, nutrition, and even genetics (Hoare & Lim, 2006; Menéndez et al., 2010; Pletz, Rohde, Welte, Kolditz, & Ott, 2016; Simonetti, Viasus, Garcia Vidal, & Carratal, 2014).

Definitions, PSI and CURB-65 score

- **Pneumonia**

Pneumonia is defined as an acute inflammatory process of lung tissue (pulmonary parenchyma) due to an infectious agent that develops in the first 48-72 hours of hospital admission. It is a common condition, and its attack rates are highest among persons at the extremes of age, including a child and elderly (J.J. Martín Villasclaras, A. Padilla Galo, 2009; Lamotte & Vicente, 2017; Marrie, 2014).

Pneumonia is generally classified as typical or atypical. Typical pneumonia is from the acute onset, meaning symptoms change or worsen quickly. Primarily is characterized by symptoms such as high fever, chills, productive cough, and pleuritic-type chest pain. At the same time, it also presents tachypnea, tubal murmur, and crackles. Usually, a chest x-ray is enough to confirm this pathology. On the other hand, atypical pneumonia is characterized by being subacute; that is, it develops more quickly than a chronic injury, but it does not become acute. The symptoms are mainly unproductive cough, fever without chills, headache, nausea, vomiting, diarrhea, myalgia, arthralgia, of several days of evolution, more evident in young people. Some of the microorganisms that produce it are: Mycoplasma, Chlamydia, and respiratory viruses (Gil, Gálvez, Sánchez, & Velasco, 2011; Palencia Vizcarra & Palencia Díaz, 2014; Rosero, 2013). Nevertheless, this classification is currently not widely used because it makes it challenging to identify the microorganism that causes pneumonia.

Instead, the classification due to the place of acquisition is used. Mainly due to the ability to identify the pathogen. Currently, this classification is most used within hospitals: community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), and healthcare-associated pneumonia (HCAP). In this case, CAP differs from the other classifications by being the most common and by characteristics such as occurrence before 48 hours of hospital admission. As long as it is in patients who have not been diagnosed with HCAP. That is, the place of acquisition of CAP is outside the hospital (Anand & Kollef, 2009). The present study is focused only on CAP owing to it is the most common class of pneumonia and, a more representative study group can be achieved.

- **Pneumonia severity index (PSI) or PS-Index**

Since the diagnosis of CAP has been widely studied, tools have emerged for many years to catalog the risk of patients diagnosed with CAP and establish whether outpatient therapy or necessary hospitalization is required. The so-called Pneumonia Severity Index score (PSI) arises from a study conducted in 14,199 adult inpatients with community-acquired pneumonia from various hospitals in the United States and sometimes called 'Fine-scale' calling its principal author. This score addresses demographic factors (age and sex), nursing home resident, coexistent illness (neoplastic disease, liver disease, congestive heart failure, cerebrovascular disease, and renal disease), physical examination aspects (mental status, respiratory rate, pressure systolic, temperature, and pulse), up to the laboratory and radiological findings (arterial pH, blood urea nitrogen, sodium, glucose, hematocrit, the partial pressure of oxygen and pleural effusion). This cohort study provides a prediction rule with 30-day hospital mortality with a score created from established values derived in 5 different classes of risk groups. Class 1 and 2 classified as outpatient management, class 3 with outpatient management or brief patient, and finally group 4 and 5 inpatient management (Fine et al., 1997).

- **CURB-65**

Years later, a score called CURB-65 was developed, where studies in the UK, New Zealand, and the Netherlands were combined. Unlike the PSI-score in CURB-65, few predictive variables are taken, which are: confusion, urea, respiratory rate, blood pressure, and age. This study achieves more precision than predecessor scales on which it is based as CRB and CRB-65 which does not include urea and uses only clinical parameters (Aujesky et al., 2005; Dwyer et al., 2014; Lim et al., 2003; Miranda Candelario, Espino Huaman, Miranda Cabrera, Cabrera Hipolito, & Rivas Rojas, 2015). In this case, the CURB-65 scale is divided into six classes assigning 1 point to each variable that exceeds the established ranges of the model. Group 0 or 1 is suitable for home treatment; group 2 is needed to consider supervised hospital treatment and group 3,4, and 5 that requires hospitalization (Lim et al., 2003). CURB-65 and PS-index scores have been widely validated by multiple risk cohort studies (Ewig et al., 2004; Zhang et al., 2018).

Diagnosis

General symptoms that characterize CAP it ranges from fever or abnormally low temperatures, signs of lower respiratory tract infection, an abnormal serum leukocyte count (leukocytosis), tachypnea, continuous sputum production in the absence of oropharyngeal irritation and rhinorrhea, with signs of condensation of the alveolar space, along with the presence of pulmonary infiltrates on the chest x-ray (America, America, & McIntosh, 2002; Shaaban & Ahmed, 2015; Simonetti et al., 2014). Depending on the severity of symptoms of CAP, there are various diagnostic supports according to the protocols established within the hospital or specialist criteria such as chest X-ray in posteroanterior (PA) and lateral view, hematic biometry and renal function, sputum analysis, arterial blood gas, biomarkers, blood cultures, pleural fluid, antigens, serology for atypical, nasopharyngeal aspirate and bronchoscopy (Gil et al., 2011; Hoare & Lim, 2006; Mandell et al., 2007; Menéndez et al., 2010; Musher & Thorner, 2014; Pletz et al., 2016; Rosero, 2013)**.** To estimate the severity of the condition, according to the HQSUR CAP protocol, the PSI and CURB-65 scores are used.

PROBLEM STATEMENT

Currently, the studies that exist in Ecuador related to pneumonia have generally been developed around the population of children under five years of age, due to pneumonia and influenza are the third cause of mortality in infants in the country. In adult populations and older adults, this kind of studies is minimal even though pneumonia and influence ranks 4th as a cause of general mortality in Ecuador (Instituto Nacional de Estadística y Censos INEC, 2019). Therefore, pneumonia management protocols of Ecuadorian hospitals are mostly based on studies carried out outside the country, where there is not the same social context, living conditions, and nutrition. Risk scores (PSI or CURB-65) are generally used to classify patients at risk and whether they are admitted to the hospital. At the same time, several studies in different countries and health centers have found variables that enhance the specificity and sensitivity of the scores, improving their prediction at the time of rating the risk of a patient.

Such is the case proposed by medical doctor Yalcin Golcuk in a study carried out in Manisa, Turkey. In which the specificity and sensitivity of the CURB-65 score are improved considering the mean platelet volume (MPV) from an established cut-off point (<8.55 fL) in the studied population (Golcuk, Golcuk, Bilge, Irik, & Dikmen, 2015). Similarly, the Department of Internal Medicine of Assaf Harofeh Medical Center in Zerifin, Israel, shows to support this theory of a rise in MPV during hospitalization by CAP in a retrospective observational cohort study (Gorelik et al., 2017). Going even further east, at Zhejiang University School of Medicine, Hangzhou, China. A study carried out where the CURB-65 score was expanded by adding lactate dehydrogenase, platelet, and albumin, thus achieving even an improvement in the risk allocation than the PSI score with much fewer variables taken into account (J. L. Liu et al., 2016). Even many times, it is only necessary to modify the values of the variables within the scores. Norfolk & Norwich University Hospital shows how modifying CURB-65 values improve specificity by up to 10% (Myint, Kamath, Vowler, & Harrison, 2007).

Therefore, these scores can be modified to obtain better precision around a defined population. When health personnel decide whether or not a person is at risk and whether or not their hospitalization is adequate, the classification capacity is improved. There is an improvement in risk allocation that potentially results in saving lives. However, there are also

secondary outcomes such as saving time and money costs in unnecessary treatments when a patient is not in an actual risk group. Modifying widely used scores and adapting them to specific groups results in a better way to establish hospital protocols according to the population that needs them. For example, PS-Index and CURB-65 are used in predicting mortality in patients with COVID-19 (a type of atypical pneumonia); however, it has been shown that adding an extra risk factor of C-reactive protein (CRP) as a variable to the PSI score, this improves its rate of risk allocation comparing only with PSI and CURB-65 (Satici et al., 2020).

Hence, the search for external factors that can help the correct risk classification of patients with pneumonia is essential to improve protocols of Ecuadorian hospitals, thus achieving an improvement in the quality of the health service. It should be noted that the few existing studies in Ecuador are related to CAP's prediction (control and CAP patients' cohorts), but not studies of risk factors within patients with CAP. Similarly, many of the studies are only observational.

OBJECTIVES

General

- To found risk factors associated with mortality in patients with community-acquired pneumonia in an Ecuadorian population.

Specifics

- To establish differences between groups of survivors and non-survivors' patients comparing socio-demographics, vital signs, comorbidities, and laboratory results variables.
- To analyze which of the standardized CAP risk scores have better accuracy in a prediction.
- To determine external factors to those used in risk scores in such a way to improve them efficacy.
- To construct a model able to predict the risk of death from CAP.

METHODOLOGY

Study design and setting

A cross-sectional retrospective cohort study was carried out in adult patients older than 21 years with a CAP diagnosis from the Hospital del IESS Quito Sur (HQSUR) in November and December 2018. It should be considered that HQSUR is a third-level public hospital considered one of the leading health centers of Quito, Ecuador. This study was carried out under the "Ley Orgánica de Protección de Datos Personales" for scientific research purposes only. Data used in this research are completely anonymous and there is no information that identifies or makes identifiable legal entities.

Selection of participants

Analyses were performed on 530 electronic health records of patients (EHR) hospitalized for respiratory diseases between November and December of 2018. The exclusion criteria for selecting patients were mainly based on the community acquired pneumonia protocol used within HQSUR. For the diagnosis of diseases, the hospital is managed according to the International Classification of Diseases, 10th edition (ICD-10). In this study, pneumonia diagnosticated patients are included, without taking into account other classes of pneumonia such as: healthcare-associated pneumonia (HCAP), hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP).

The criteria for patient exclusion were made in 3 steps: 1) Rule out patients' diagnosis with other respiratory diseases, no available data and patients without chest X-ray (CXR) confirmation of CAP. 2) Younger than 21 years. 3) Patients diagnosed with another kind of pneumonia rather than CAP. The number of patients by exclusion criteria can be seen in detail in the diagram of appendix section. No immunosuppressed, pregnant or previously hospitalized patients.

Data collection

The information was obtained from the EHR of each filtered case, for which a database of 84 patients with CAP was created taking clinical data which include patient's demographic, clinical presentation, comorbidity, vital signs and laboratory information within the first 48 hours of hospital admission, where the groups of variables under study were registered as follows:

Sociodemographic variables

For variable age, it is considered all patients ranging from the youngest patient 21 years to the oldest 96 years old. The gender variable is taken as dichotomous (female, male). Same for the variables of alcoholism and smoking (yes, no).

Vital signs variables

The vital sign variables are constituted by corporal temperature measured in degrees centigrade (°C), heart rate measured in beats per minute (bpm), respiratory rate measured in breaths per minute (bpm), oxygen saturation which indicates the level of oxygen in blood in percentage (%) and systolic and diastolic blood pressure measured in millimeters of mercury (mm Hg).

Comorbidities or clinical conditions

In total, more than 200 comorbidities were found within the clinical records. Because of the specificity of these diseases and clinical conditions, it is decided to group them into a more general group according to their ICD-10 classification code, for example in the case of hyperosmolality and hypernatremia (E87.0), hypo-osmolality and hyponatremia (E87.1), hypokalemia (E87.6) and other disorders of electrolyte and fluid balance, not elsewhere classified (E87.8) where associated in a general category of other disorders of fluid, electrolyte and acid-base balance (E87) in such a way to generate a representative quantity of a general disease.

Once the corresponding groups of diseases are generated, it is decided to only take into account the most common and representative diseases found which are: diabetes mellitus, mental disorders, renal failure, septic shock, cerebrovascular disease, respiratory failure, pleural effusion, hepatic disease, essential (primary)

hypertension, other forms of heart disease, dependence on renal dialysis, cystitis and other disorders of fluid, electrolyte and acid-base balance.

Laboratory results: Hemogram

Continuous variables of white blood cells (WBC), hemoglobin (HGB), hematocrit (HCT), mean cell volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width - standard deviation (RDW-SD), mean platelet volume (MPV), monocytes (MO), eosinophils (EOS), lymphocytes (LY), neutrophils (NE), basophils (BAS), platelet (PLT), red blood cell count (RBC), red cell distribution width - coefficient of variation (RDW-CV), platelet distribution width (PDW) were included in the hematic biometry tests (LabCE, 2020).

Monocytes, eosinophils, lymphocytes, neutrophils, and basophils were included both in absolute (abs) and in their respective percentages (pct.) as well.

Laboratory results: Biochemistry, blood electrolytes and arterial gasometry

The following variables were included in the biochemical analysis: glucose (Glu), blood urea nitrogen (BUN), and creatinine (Cr), for the blood electrolytes, were included: chloride (Cl^-), potassium (K^+) and sodium (Na^+).

In the case of arterial gasometry were included: partial pressure of carbon dioxide (PCO_2), the partial pressure of oxygen (PO_2), bicarbonate in the blood (HCO_3^-), oxyhemoglobin saturation (SO_2), base excess (BE) and blood lactate (BL) were included with their respective abbreviations (Barhum, 2018).

Categorization of variables

Variables that showed significant differences between groups of survivors and non-survivors were categorized according to their low, normal, and high values, based on sex and age of patients. Reference tables from AHS Laboratory Services and Marshfield Labs were used primarily. References were compared with normal values of hemograms of people in the northern part of Ecuador (AHS Laboratory Services, 2018; CLL Society, 2016; Dugdale, 2019; Flor, G, & Cruz, 2008; Scherr, 2013)**.**

Statistical analysis

Descriptive statistics used for continuous variables were mean and standard deviation and for categorical variables, frequency, and percentages according to their corresponding group. Kolmogorov-Smirnov test was used to check the normality of continuous variables (age, vital signs, laboratory tests), except in cases of small sample sizes ($n \leq 50$) where instead a Shapiro-Wilk test was used. For the comparison of categorical variables (sex, alcoholism, smoking, comorbidities or clinical conditions, and class scores), Fisher's exact test was used. Continuous variables normally distributed were compared by the t-student test, while continuous non-normally distributed variables were compared using the Mann-Whitney U test. Simple Logistic Regression (SLR) was performed to explore the association of clinical characteristics and categorized variables of laboratory parameters. A model using Multiple Logistic Regression (MLR) is proposed using mortality by CAP as the dependent variable and those that were significantly associated with the previous analyzes as covariates. For all analyses, a two-tailed test for alpha less than 0.05 was considered to indicate statistical significance. Data analysis was performed in the statistical software SPSS version 25 for Windows.

RESULTS AND DISCUSSION

Missing data on EHR

The vital signs variables were taken into account if they did not exceed 10% loss, except for the temperature variable, which had a loss of 16.7%. On the other hand, variables related to laboratory tests had different percentages of missingness, which is why it is elected to show the samples' size in all cases. For the rest of the demographic and comorbidity variables or clinical conditions, there was no missingness of information (See Appendix Table 1 for details). The variables used to create the binary logistic regression model are within an established limit of not exceeding 20% data loss.

Analysis of the CAP risk factors

This study was carried out with a total of 84 patients (38 men and 46 women) with a principal diagnostic of CAP, in which 64 patients (74.6%) recovered (survivor group) and the remaining 19 patients (22.6%) were in-hospital mortality (non-survivor group). Due to the closeness of both cohorts (all patients diagnosed with CAP); it is expected to find a few variables that show a significant difference between both groups. Only 9 of the 60 variables used in this study showed a significant difference; therefore, the rest of the variables were neglected.

Demographic characteristics of the patients, as well as their vital signs, are described in Table 1, where age was the only variable that showed a significant difference, in the case of the group of non-survivors with a significance of $P = 0.002$.

Table 1. Sociodemographic characteristics and vital signs of the patients.

Variables	Survivors (n = 65)	Non-survivors (n = 19)	*P*-value
Demographic findings:			
Age (yr): Mean ± SD	68.68 ± 20.55	83.63 ± 8.47	**0.002**
Sex (M): No. (%)			0.799
Female	35 (53.8)	11 (57.9)	
Male	30 (46.2)	8 (42.1)	
Alcoholism: No. (%)	28 (43.1)	8 (42.1)	1.000
Smoking: No. (%)	3 (4.6)	0 (0)	1.000
Vital signs: Mean ± SD			
Temperature (°C)	36.72 ± 0.74	36.79 ± 0.99	0.955
Heart rate (bpm)	85.66 ± 19.39	92.58 ± 22.84	0.193
Respiratory rate (bpm)	19.45 ± 3.24	19.82 ± 3.89	0.889
Oxygen saturation (%)	89.66 ± 4.59	89.63 ± 5.38	0.674
Systolic blood pressure (mmHg)	120.51 ± 25.69	123.63 ± 19.58	0.626
Diastolic blood pressure (mmHg)	68.14 ± 13.87	65.16 ± 15.58	0.425

-Significant *P*-values are in bold letter.

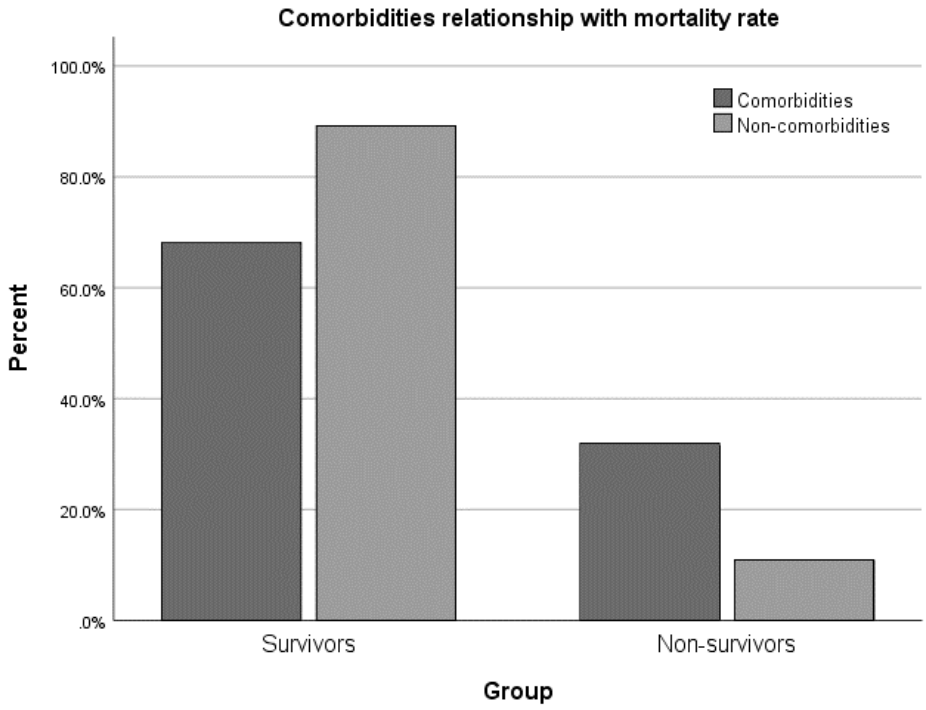
In the section of comorbidities or clinical conditions in Table 2, only 2 conditions were found significant, mental disorders (7.7% vs 31.6%, $P = 0.014$) and cystitis disease (7.7% vs 26.3%, $P = 0.040$). Figure 1 shows the difference between patients without comorbidities and mortality concerning patients who do, where it can quickly see that more than twice the number of patients in the non-survivor group has one or more comorbidities.

Table 2. Clinical signs and comorbidities within the first 48 h of admission.

Variables	Survivors (n = 65)	Non-survivors (n = 19)	*P*-value	RR	95% CI	
					Lower	Upper
Clinical conditions: No. (%)						
Diabetes mellitus	10 (15.4)	5 (26.3)	0.313	1.964	0.578	6.676
Other disorders of fluid, electrolyte and acid-base balance	5 (7.7)	3 (15.8)	0.373	0.250	0.049	10.432
Mental disorders	5 (7.7)	6 (31.6)	**0.014**	5.538	1.465	20.935
Essential (primary) hypertension	9 (13.8)	3 (15.8)	1.000	1.167	0.282	4.826
Other forms of heart disease	5 (7.7)	3 (15.8)	0.373	0.025	0.049	10.432
Liver disease	2 (3.1)	0 (0)	1.000			
Renal failure	5 (7.7)	4 (21.1)	0.199	3.200	0.765	13.390
Cystitis	5 (7.7)	5 (26.3)	**0.041**	4.286	1.090	16.854
Septic shock	7 (10.8)	2 (10.5)	1.000	0.975	0.185	5.136
Dependence on renal dialysis	1 (1.5)	2 (10.5)	0.127	7.529	0.644	88.069
Respiratory failure	19 (20.0)	8 (42.1)	0.071	2.909	0.973	8.695
Cerebrovascular disease	1 (1.5)	1 (5.3)	0.403	3.556	0.212	59.693
Pleural effusion	1 (1.5)	2 (10.5)	0.127	7.529	0.644	88.069
Hepatic disease	6 (9.2)	0 (0)	0.329			

-Significant *P*-values are in bold letter.

Figure 1. Bar chart of comorbidity in relation to in hospital mortality.



The bar chart shows percentages of patients in the groups of comorbidities.

In the same way for laboratory exams such as hemogram, it is possible to appreciate in Table 3 some variables showing significant differences, which are HGB with $P = 0.021$, HCT with $P = 0.026$, RBC with $P = 0.020$ and pct. of monocytes with $P = 0.039$.

Table 3. Hemogram values.

Variables	Survivors		Non-survivors		*P*-value
	n	Mean ± SD	n	Mean ± SD	
Hemogram:					
WBC (K / µL)	65	9.21 ± 3.93	18	9.23 ± 5.14	0.749
HGB (g / dL)	63	14.02 ± 2.89	17	12.19 ± 2.64	**0.021**
HCT (%)	65	41.97 ± 8.83	18	36.73 ± 7.89	**0.026**
MCV (fL)	54	90.69 ± 5.90	17	91.00 ± 4.46	0.843
MCH (pg)	54	30.31 ± 2.47	15	30.41 ± 1.52	0.856
MCHC (g / dL)	54	33.35 ± 1.25	15	33.22 ± 1.11	0.305
RDW – SD (fL)	47	46.69 ± 6.15	14	49.68 ± 11.09	0.150
MPV (fL)	52	9.69 ± 1.06	15	9.48 ± 1.51	0.535
Monocytes (K / µL)	53	0.59 ± 0.30	15	0.53 ± 0.35	0.375
Eosinophils (K / µL)	53	0.08 ± 0.12	15	0.08 ± 0.10	0.736
Lymphocytes (K / µL)	53	1.21 ± 0.70	15	1.05 ± 0.65	0.314
Neutrophils (K / µL)	54	7.74 ± 3.99	16	8.06 ± 4.84	0.983
Basophils (K / µL)	53	0.03 ± 0.02	16	0.04 ± 0.03	0.466
Platelet (K / µL)	63	221.60 ± 104.82	18	248.50 ± 117.82	0.315
RBC (M / µL)	56	4.65 ± 1.03	16	3.98 ± 0.85	**0.020**
Monocytes (%)	55	6.46 ± 2.22	16	5.47 ± 3.53	**0.039**
Eosinophils (%)	56	1.11 ± 1.60	16	0.93 ± 1.21	0.973
Lymphocytes (%)	58	15.51 ± 10.55	17	11.89 ± 6.63	0.366
Neutrophils (%)	60	76.19 ± 12.29	18	81.93 ± 10.27	0.087
Basophils (%)	53	0.34 ± 0.26	16	0.44 ± 0.41	0.474
RDW – CV (%)	49	14.47 ± 2.33	15	15.24 ± 2.87	0.111
PDW (%)	45	16.10 ± 0.53	14	16.06 ± 0.38	0.759

-Significant *P*-values are in bold letter.

In the biochemistry examination, no variable showed a significant difference. Conversely, the electrolyte exams in blood show a clear difference in a decrease of Na in the group of non-survivors with $P = 0.044$. In the arterial gasometry tests, the only variable that showed a significant difference was that of blood lactate with a considerable rise with $P = 0.044$ (See Table 4).

Table 4. Biochemistry, electrolytes in blood and arterial blood gas values.

Variables	Survivors		Non-survivors		*P*-value
	n	Mean ± SD	n	Mean ± SD	
Biochemistry examination:					
Glucose (mg/dL)	28	122.01 ± 42.93	7	173.66 ± 138.56	0.564
Blood urea nitrogen (mg/dL)	24	60.72 ± 46.29	5	54.30 ± 27.12	0.862
Creatinine (mg/dL)	39	1.35 ± 1.37	11	2.01 ± 1.50	0.092
Blood electrolytes:					
Chloride (mg/dL)	50	104.59 ± 6.10	17	102.32 ± 10.11	0.280
Potassium (mg/dL)	50	3.98 ± 0.93	17	4.13 ± 0.78	0.363
Sodium (mg/dL)	50	137.78 ± 6.09	17	134.25 ± 9.38	**0.044**
Arterial gasometry:					
Arterial pH	39	7.42 ± 0.08	8	7.40 ± 0.09	0.514
PCO_2 (mmHg)	39	33.39 ± 7.47	8	33.64 ± 10.88	0.989
PaO_2 (mmHg)	39	63.29 ± 19.97	8	75.38 ± 33.38	0.153
HCO_3^- (mEq / L)	39	20.79 ± 3.30	8	20.05 ± 5.87	0.737
SO_2 (%)	39	86.68 ± 9.81	8	84.75 ± 22.76	0.697
BE	38	-2.86 ± 3.59	8	-3.95 ± 5.53	0.460
BL (mmol / L)	37	1.71 ± 0.58	8	2.39 ± 0.97	**0.044**

-Significant *P*-values are in bold letter.

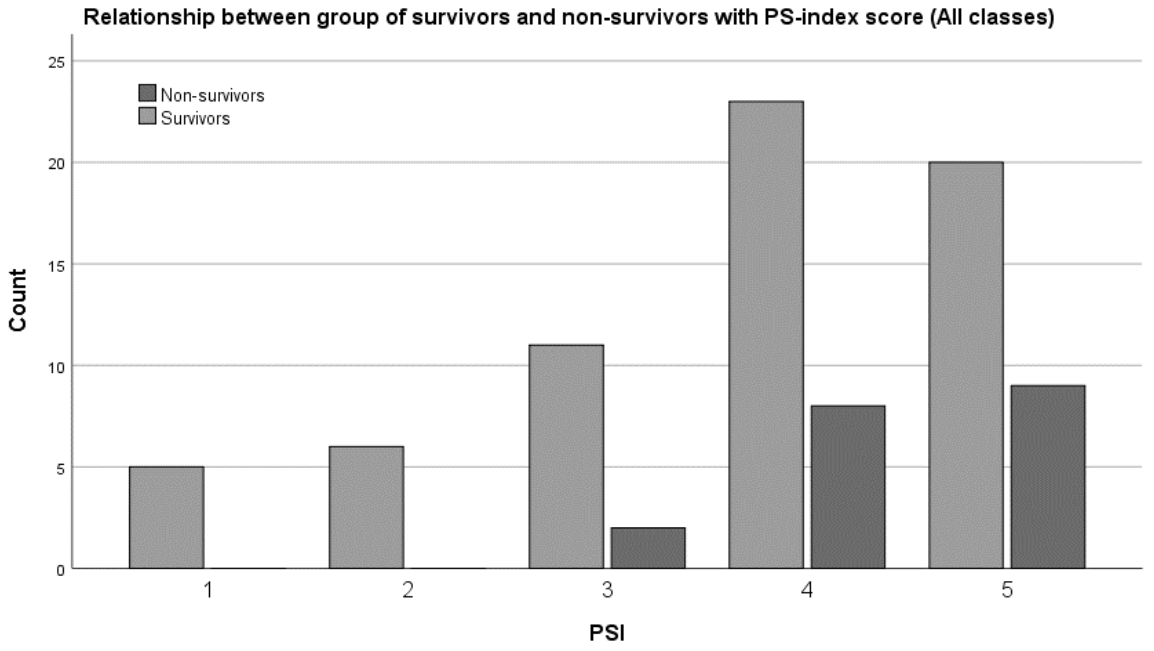
As regards assign severity assessment of CAP patients; Cross-reference in Table 5 reveal that both the PS-index and CURB-65 scales do not show any deceased in their respective low-risk scores. Else, score ≥ II shows the highest risk of the CURB-65 scale, showing a significance between risk classes of $P = 0.017$. Comparatively, the PS-index score also shows a high mortality rate in score IV & V, showing that 89.5% of deceased patients belong to this group, disclosing a significance of $P = 0.028$. The classification of all risk classes using PSI and CURB-65 scores can be evidenced in Figure 2 and Figure 3 respectively. Particular attention should be paid to the CURB-65 score, where the difference is graphically appreciated from class 1 onwards. Class I shows a difference of almost 3:1 of deaths concerning the group of survivors, class II shows a 2:1 difference and finally in a class III relation of 2:3.

Table 5. PS-index and CURB-65 scores in relation to mortality by CAP.

Variables	Survivors (n = 65)	Non-survivors (n = 19)	*P*-value
CURB-65 Score: No. (%)			**0.017**
CURB-65 0	16 (24.6)	0 (0)	
CURB-65 I	29 (44.6)	9 (47.4)	
CURB-65 II	17 (26.2)	8 (42.1)	
CURB-65 III & IV & V	3 (4.6)	2 (10.5)	
PS-index Score: No. (%)			**0.028**
PS-index I & II	11 (16.9)	0 (0)	
PS-index III	11 (16.9)	2 (10.5)	
PS-index IV & V	43 (66.2)	17 (89.5)	

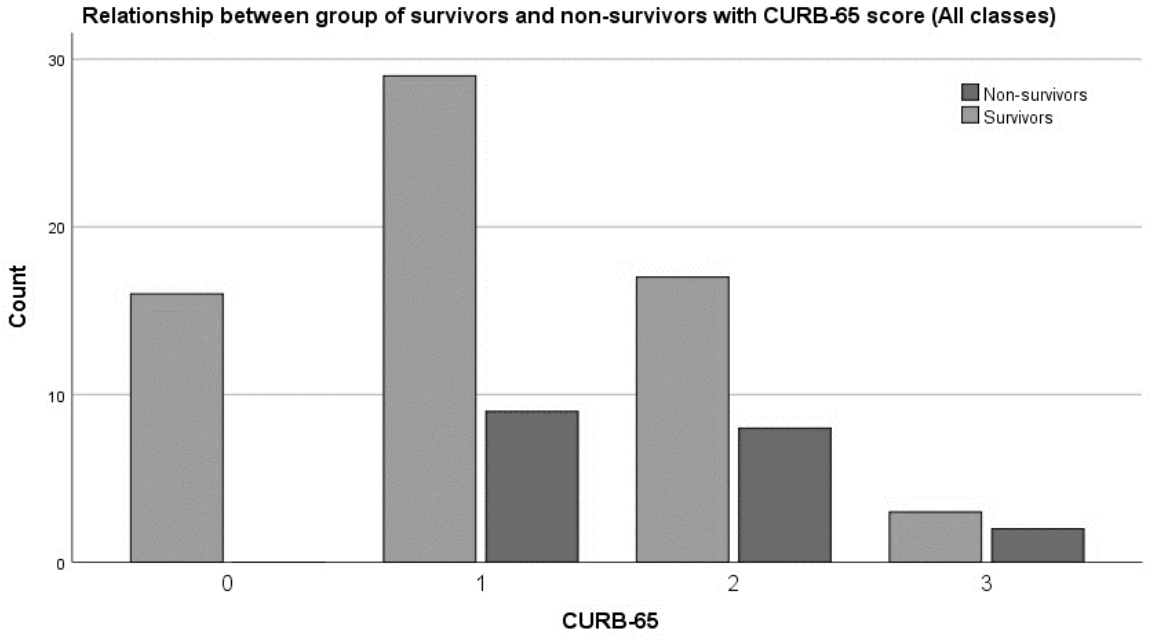
-Significant P-values are in bold letter; No patient with scores IV & V in CURB-65.

Figure 2. Bar chart of PSI score in relation to patients.



The bar chart represents the number of patients inside the classification of PS-Index score.

Figure 3. Bar chart of CURB-65 score in relation to patients.



The bar chart represents the number of patients inside the classification of CURB-65 score.

Categorization of significantly different variables between groups

The continuous variables that showed differences between groups were categorized using reference values divided into three sections (low, normal, high), taking into account the sex of the patients studied. Each category is represented by a number 0 for low, 1 for medium, and 2 for high. In such a way, create three levels of each variable that considers the differences existing for the subgroups of men and women. Simultaneously, due to the limited sample, an attempt is made to cover a broader range than established cut-off points by risk factors.

In other words, for hematocrit levels each measurement is separated concerning sex and its respective survival group. This categorization is carried out since the cut-off point for the HCT to consider it a risk factor is <30% according to the PS-Index score. However, due to the sample size limitation, this reference range is not taken, but rather a value that is below the normal ranges for men and women. The same process is carried out for the HGB and RBC. However, as there are no differences between groups of men and women concerning sodium and BL, it is used in the normal reference range. In the case of sodium, the PS-Index score takes it as a risk factor if it is less than 130 mmol / L, nevertheless is not used. No classification is made for the variables of age and percentage of monocytes. For the age variable, it is due to the only people who died are in a single group of ≥ 65, and for pct. of monocytes, there are no considerable values out of the normal range.

Crosstab of the groups of survivors and non-survivors concerning each category of significant variables (HCT, HGB, RBC, Na and BL) as well as its ORs and significance in the univariate analysis are shown in Table 6. The results of the SLR make it possible to compare categorized variables of the laboratory in a group of patients who died from CAP versus those who were discharged alive. It is found that the variables of low hematocrit, low hemoglobin, low red blood cell counts, low sodium levels and high blood lactate were statistically significantly associated, showing a direct risk relationship. On the other hand, showing a protective action, normal levels of sodium and lactate in the blood were significant.

Table 6. Categorization, crosstabs, ORs and P-values of significantly different variables.

Variable	Category	Survivors No. (%)	Non-survivors No. (%)	P-value	Odds ratio (95% CI)
HCT	Low (0)	17 (26.2)	10 (55.5)	**0.025**	3.529 (1.196 - 10.412)
	Normal (1)	34 (52.3)	7 (38.9)	0.426	0.580 (0.200 - 1.684)
	High (2)	14 (21.5)	1 (5.6)	0.172	0.214 (0.026 - 1.753)
HGB	Low (0)	17 (27.0)	10 (58.8)	**0.021**	3.866 (1.268 - 11.784)
	Normal (1)	33 (52.4)	7 (41.2)	0.586	0.636 (0.215 - 1.883)
	High (2)	13 (20.6)	0 (0)	0.06	7.46 (0.649 - 0.858)
RBC	Low (0)	13 (23.2)	9 (56.2)	**0.028**	4.253 (1.352 - 13.653)
	Normal (1)	29 (51.8)	6 (37.5)	0.399	0.559 (0.179 - 1.746)
	High (2)	14 (25.0)	1 (6.3)	0.164	0.200 (0.024 - 1.654)
Na	Low (0)	13 (30.2)	11 (68.8)	**0.015**	5.077 (1.467 - 17.568)
	Normal (1)	25 (58.1)	4 (25.0)	**0.039**	0.240 (0.066 - 0.866)
	High (2)	5 (11.7)	1 (6.2)	1	0.507 (0.055 - 4.706)
BL	Normal (1)	5 (13.5)	5 (62.5)	**0.007**	0.940 (0.170 - 5.200)
	High (2)	32 (86.5)	3 (37.5)	**0.007**	10.667 (1.922 - 59.200)

-Significant P-values are in bold letter; CI, confidence interval.

Multivariate Binary Logistic Regression model of CAP risks factors

The MLR analysis provides information on which variables can be used as predictors of CAP mortality. Each covariate in the model previously displayed statistical significance in the difference between non-survivors and survivors in the univariate analysis. Besides, all the covariates used was in at least 80% complete. The variables corresponding to each section introduced in the model were age in sociodemographic aspects; mental brain disorders (MD) in comorbidity or clinical conditions; the percentage of monocytes, RBC and HGB for laboratory's exams. Table 7 shows which variables were statistically significant for the multivariate model.

Table 7. Multivariate logistic regression analysis of mortality risk factors for patients with CAP

Variables	B	S.E.	Wald	df	*P*-value	Odds Ratio	95% CI	
							Lower	Upper
Age	0.064	0.029	4.939	1	**0.026**	1.067	1.008	1.129
Monocytes (%)	0.018	0.132	0.018	1	0.894	1.018	0.786	1.318
MD	2.087	0.974	4.590	1	**0.032**	8.060	1.194	54.384
RBC (Low)	1.324	1.617	0.671	1	0.413	3.760	0.158	89.375
HGB (Low)	1.055	1.554	0.461	1	0.497	2.872	0.136	60.439
Constant	-7.747	2.709	8.180	1	0.004	0.000		

-Significant *P*-values are in bold letter; B, Regression coefficient; S.E., Standard error; Wald, Test de Wald; df, degrees of freedom; CI, confidence interval; MD, mental disorders; RBC, red blood count; HGB, hemoglobin.

Likelihood of dying from CAP was reckoned by the following equation:

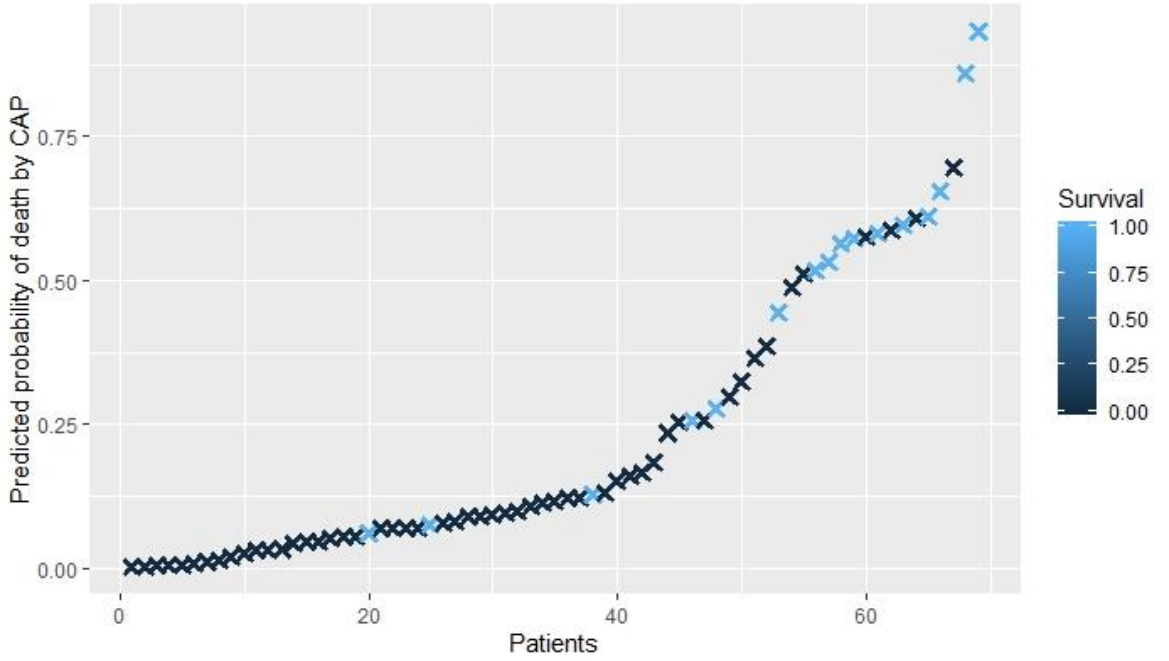
$$\hat{y} = -7.747 + (0.064) * \text{Age} + (0.018) * \text{Monocytes (\%)} + 2.087 * \text{MD} + 1.324 * \text{RBC (Low)} + 1.055 * \text{HGB (Low)}$$

Note: The overall success rate of the model was 84.1%.

$\hat{y}$ = Predicted logit score for non-survivor group

Age and having a mental disorder were positively associated with the probability of dying from CAP. The older the age of a patient (base 21 years), the greater the risk of belonging to the group of non-survivors (OR: 1.067; 95% CI: 1.008-1.129; *P* = 0.026), in the same way, the presence of mental disorders in a patient increases the risk (OR: 8.060; 95% CI: 1.194-54.384; P = 0.032). See Figure 4 for graphic results of the model.

Figure 4. Graphic results of logistic regression



Graphical diagnosis of the model that shows the patients with the probability of dying by CAP. Where 0 represents the group of survivors and 1 represents the group of non-survivors.

Simulations based on the estimated equation:

Example 1. What is the risk of dying from CAP in a 91-year-old patient with mental illness, low HGB, low RBC and pct. of monocytes of 3.2? Answer = deceased patient.

$$\hat{y} = -7.747 + (0.064) * 91 + (0.018) * 3.2 + 2.087 * 1 + 1.324 * 1 + 1.055 * 1$$

$$\hat{y} = 2.601$$

Inverse Logit Function:

$$\mu = \frac{1}{1 + e^{-\hat{y}}}$$

μ is the probability that the outcome equals to 1. Where 0 represents survivor group and 1 non-survivor group.

Note: Equation used to transform from logit score (obtained in the binary logistic regression model) to probability.

$$\mu = \frac{1}{1 + e^{-2.601}} = 0.933$$

Result: Chances of death of the patient 93.3% or considered as patient in group 1.

Example 2. What is the risk of dying from CAP in an 86-year-old patient with no mental illness, no low HGB, no low RBC and pct. of monocytes of 9.5? Answer = survivor.

$$\hat{y} = -7.747 + (0.064) * 86 + (0.018) * 9.5 + 2.087 * 0 + 1.324 * 0 + 1.055 * 0$$

$$\hat{y} = -2.072$$

$$\mu = \frac{1}{1 + e^{-(-2.072)}} = 0.115$$

Result: Chances of death of the patient 11.5% or considered as patient in group 0.

Example 3. What is the risk of dying from CAP in an 80-year-old patient with mental illness, low HGB, no low RBC and pct. of monocytes of 5.3? Answer = deceased patient.

$$\hat{y} = -7.747 + (0.064) * 80 + (0.018) * 5.3 + 2.087 * 1 + 1.324 * 0 + 1.055 * 1$$

$$\hat{y} = 0.6104$$

$$\mu = \frac{1}{1 + e^{-(-2.072)}} = 0.655$$

Result: Chances of death of the patient 65.5% or considered as patient in group 1.

Risk assessment is a fundamental tool in the management of a patient with CAP. PS-Index and CURB-65 are among the most widely used scores to catalog different classes of risk in CAP. Both being widely used due to their multiple validations and easy calculations in practice (Ewig et al., 2004). From this, it is possible to stratify the patients according to their risk of death or the most appropriate treatment intensity. Although both scores work relatively well with strengths and weaknesses, modifications in the cut-off points or even taking additional aspects, the risk prediction can be considerably improved (Buising et al., 2006; J. H. Chen et al., 2010). Many times, depending on the case, such as patients in ICU, other predictive scores work in a better way (Eldaboosy et al., 2015). In this work it is possible to verify the effectiveness of the PS-Index and CURB-65 scores at the time of cataloging the risk of a patient with CAP within the HQSUR. Similarly, it can be seen that mortality (22.6%) is high compared to other similar studies (Bauer, Ewig, Marre, Suttorp, & Welte, 2006; Lee et al., 2016). Nonetheless, researches with small samples sizes ($n \leq 100$) report similar results (Shaaban & Ahmed, 2015). It should be noted that studies in countries close to Ecuador the general mortality rate do not show any difference, such as the case proposed by Machado Alba, Isaza, & Sepúlveda in a tertiary hospital in Colombia (2013).

The findings related to sociodemographic aspects show only significant differences in the age of the patients. Being the age of the mortality group (83.63 ± 8.47 years) similar to that of several studies reported (Baik et al., 2000; Dang, Eurich, Weir, Marrie, & Majumdar, 2014; Wójkowska-Mach et al., 2013). Male sex is considered a risk factor in the PS-Index score, which is widely validated, although it is true that there are studies that have not shown any significant difference in the incidence of CAP between sexes (Fine et al., 1997; Rivero-Calle et al., 2016). This study's results support the non-difference in the incidence of CAP for men and women like reports from Gau et al., (2010) and Dang et al. (2014). The vital signs section shows unexpected results since there is no significant difference between groups. Investigations around CAP mostly report important contrast in all the vital signs proposed in this study. These differences have favored by many studies those carried out around the world like authors declare like Shaaban & Ahmed in Egypt (2015), Fujiki et al., in Japan (2007) and Zhang et al. (2018), the latter based on cut-off points established by PSI and CURB-65 score. Despite the typical differences between the means of both groups, such as higher temperature, heart rate, respiratory rate, and lower oxygen

saturation and systolic pressure in non-survivors, none of them were significantly different. The only variable that shows a higher value when it should not be is systolic pressure in the non-survivor group.

Similarly, the section on comorbidities or clinical conditions, variables considered essential risk factors did not show significant differences. For example, it is the case of pleural effusion, cerebrovascular, kidney, liver and heart diseases which are used as risk predictor variables in the PS-Index score (Fine et al., 1997). Despite mostly negative results, two diseases showed significance in the univariate analysis these were mental disorders and cystitis.

Concerning mental disorders, an assortment of studies verifies that the risk increases considerably in patients with CAP and some mental disorders. Garcia-Vidal et al. (2008) show a prospective study carried out in Spain in 2,457 patients. They place an altered mental state as one of the main comorbidities responsible for mortality in patients with CAP. A typical result in a large number of studies, especially in elderly adults (Saldías Peñafiel, O'Brien Solar, Gederlini Gollerino, Farías Gontupil, & Díaz Fuenzalida, 2003; Waterer, Kessler, & Wunderink, 2004). Without a doubt, the presence of mental illness is an obvious risk factor. However, researches name various causes as directly responsible. The hypothesis suggests that one reason is a link between mental state and immune function, such as cytokine levels. A mental illness could result in changes in cytokine levels, resulting in an altered capacity to react against infections and other immune responses (Dinarello, 2000; Jones & Thomsen, 2013). Another possibility is that the wide range of mental illnesses increases the risk of pneumococcal disease (any infections caused by *Streptococcus pneumoniae*) which would explain a large number of CAP patients with this comorbidity (Seminog & Goldacre, 2013). Nonetheless, as it is a retrospective study carried out with clinical data, there will be no debate about its physiological reason.

On the other hand, the unexpected comorbidity, in this case, was cystitis. Although it is a somewhat strange result in CAP risk factors studies, the explanation could be more in the infecting organism. This is the case of Drs Franke & Frye (2001), who found a high incidence of the microorganism Chlamydia pneumoniae in women who suffer from interstitial cystitis. The hypothesis raised is that the microorganism first enters the alveoli

producing pneumonia. Once there, it can invade immune cells where the microorganism remains inactive until those cells are needed to fight inflammations in other areas of the body such as the bladder or near it, producing the syndrome of interstitial cystitis (Franke & Frye, 2001). Due to the limited solid research related to cystitis as a risk condition with CAP, this comorbidity is not taken into account for the subsequent prediction model.

In this study, the section on laboratory variables shows mostly expected results. This is the case of low hematocrit levels and low sodium concentration in the group of non-survivors, the last indicating hyponatremia. Both factors are considered risk within the PS-Index score (Fine et al., 1997). Low levels of hematocrit and sodium in the blood are currently important risk factors for dying from CAP (Nair, Niederman, Masani, & Fishbane, 2007; Zilberberg et al., 2008).

Although other results are not within the class scores, such as blood lactate, this is used as independent or secondary indicators of risk, especially in emergency department patients (Bou Chebl et al., 2017; Y. X. Chen & Li, 2015; Mandell et al., 2007). Factors to which special attention should be paid are hemoglobin, red blood count, and monocytes percentage because they could be indirect indicators of some clinical condition that puts the patient at risk. For example, low levels of HCT, HGB, and RBC could indicate the presence of anemia that is not reported according ICD-10 code in the group of non-survivors (Gersten, 2018; Russell & Wilson, 2017).

However, the difficulty of associating anemia as a factor lies in the diversity of studies with opposite results. Showing that anemia in adults is an independent risk factor, or neither is it (Cabrera, 2009; Doshi, Rueda, Corrales-Medina, & Musher, 2011; Reade, Weissfeld, Angus, Kellum, & Milbrandt, 2010). Even supposing this hypothesis, it should be considered to submit to a thorough review of the EHR data by a health specialist, there are some studies in Ecuador that can be an initial point. Unfortunately, all the investigations carried out within Ecuador that show that anemia is an extremely important risk factor are only in children under five years of age (Garrido Salazar, Fuseau, Garrido, Vivas, & Gutiérrez, 2018; Harris et al., 2011; Jonnalagadda et al., 2017).

Identically, some factors are not within the PS-Index and CURB-65 scores that are considered risk factors such as signs of leukopenia (low HGB levels) and thrombocytopenia (low PLT levels) (Shaaban & Ahmed, 2015; Watkins & Lemonovich, 2011). In this case, the explanation for the monocytes' percentage difference comes from the fact that monocytes are a type of agranulocyte leukocytes. Although it is also known that monocytes are at the same time influenced by and contributors to age-associated inflammation. This chronic exposure inflammation increases the risk of being infected by S. pneumoniae which is the main causative organism of CAP (Puchta et al., 2016).

Indeed, differences between survival groups do not demonstrate a causal relationship. The MLR model is proposed to identify which signs can be used as predictors of mortality from CAP in the population. This study finds two relevant factors associated with the CAP mortality group within the HQSUR. Age and mental disorder show to be essential factors when cataloging the risk status of a patient with CAP. The importance of the characteristics of age and mental disorders included in the PS-Index score and age in the CURB-65 score is reaffirmed. Likewise, the effectiveness of the two scores applied to Ecuadorian adult patients with CAP is displayed. It is important to emphasize the high mortality rate compared to studies conducted in other non-South American countries. This study shows contrasts between mortality groups that can be used in future research using a starting point, the notorious differences between blood variables as possible indicators of a linked disease.

This study's main weakness was the missing amount of data that limits the effectiveness of the proposed predictive model. Variables that could be essential predictors were not used due to the amount of data loss. Similarly, the early management of the data was based on EHR, which, to a large extent, does not follow a single format. For example, for essential clinical conditions, the ICD-10 cataloging format is used; however, the information is stored without any specific code for physical examination findings and other signs. Which finally makes it difficult to access to the physical results mentioned by medical personnel. For which it was presided to use numerical values in vital signs. Simultaneously, the study group is significantly reduced due to the filters to choose the appropriate population trying to avoid selection biases. Although it is a very limited study, its results are consistent with a cohort of patients with pneumonia with significant variables that have their clinical and physiological reason.

CONCLUSIONS AND RECOMMENDATIONS

In summary, risk factors associated with mortality of the CAP population in Ecuador were age and mental disorders. This study highlights the extreme importance of both aspects of the risk allocation of a patient with CAP. The clinical differences between survivors and non-survivors were age, HCT, Na, BL, and presence MD used as indicators of CAP severity. However, there were also factors such as HGB, RBC, and the percentage of monocytes that should be considered to be a valuable indicator of an unreported disease or condition. PS-index and CURB-65 scores show similar results at the time of risk assignment despite the population size limitation. No external factors to the scores were found that could be used as predictors of CAP mortality. The latter, because of the only two significant variables in MLR, were age and mental disorders considered risk within the PS-index score.

Even though this study's results support the risk scores used in the HQSUR CAP management protocol, it is important to emphasize that it was conducted in a reduced population. It is necessary to carry out this kind of research within the Ecuadorian public health centers in order to improve the health protocols used. Therefore, develop a better patient care public health system.

Finally, the following research avenues are recommended:

1. It is necessary to conduct a specified study around the hemogram section that shows extremely low HCT, HGB, and RBC values in the group of non-survivors, indicating a possible clinical condition such as anemia that is not reported according to ICD-10 classification.
2. This study shows positive results despite several limitations. It can be useful as a basis for future researchers in public hospitals in the country.

ABBREVIATIONS

T	Temperature
HR	Heart rate
RR	Respiratory rate
O2sat	Oxygen saturation
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
WBC	White blood cells
HGB	Hemoglobin
HCT	Hematocrit
MCV	Mean cell volume
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
RDW-SD	Red cell distribution width - standard deviation
MPV	Mean platelet volume
MO	Monocytes
EOS	Eosinophils
LY	Lymphocytes
NE	Neutrophils
BAS	Basophils
PLT	Platelet
RBC	Red Blood Cell Count
RDW-CV	Red cell distribution width - coefficient of variation
PDW	Platelet Distribution Width

Glu	Glucose
BUN	Blood urea nitrogen
CR	Creatinine
Cl^-	Chloride
K^+	Potassium
Na^+	Sodium
PCO_2	Partial pressure of carbon dioxide
PO_2	Partial pressure of oxygen
HCO_3^-	Bicarbonate in blood
SaO_2	Oxyhemoglobin saturation
BE	Base excess
BL	Blood lactate
Abs	Absolute
Pct.	Percentage
PSI	Pneumonia severity index
CURB-65	Confusion, urea, respiratory frequency, blood pressure, 65 years

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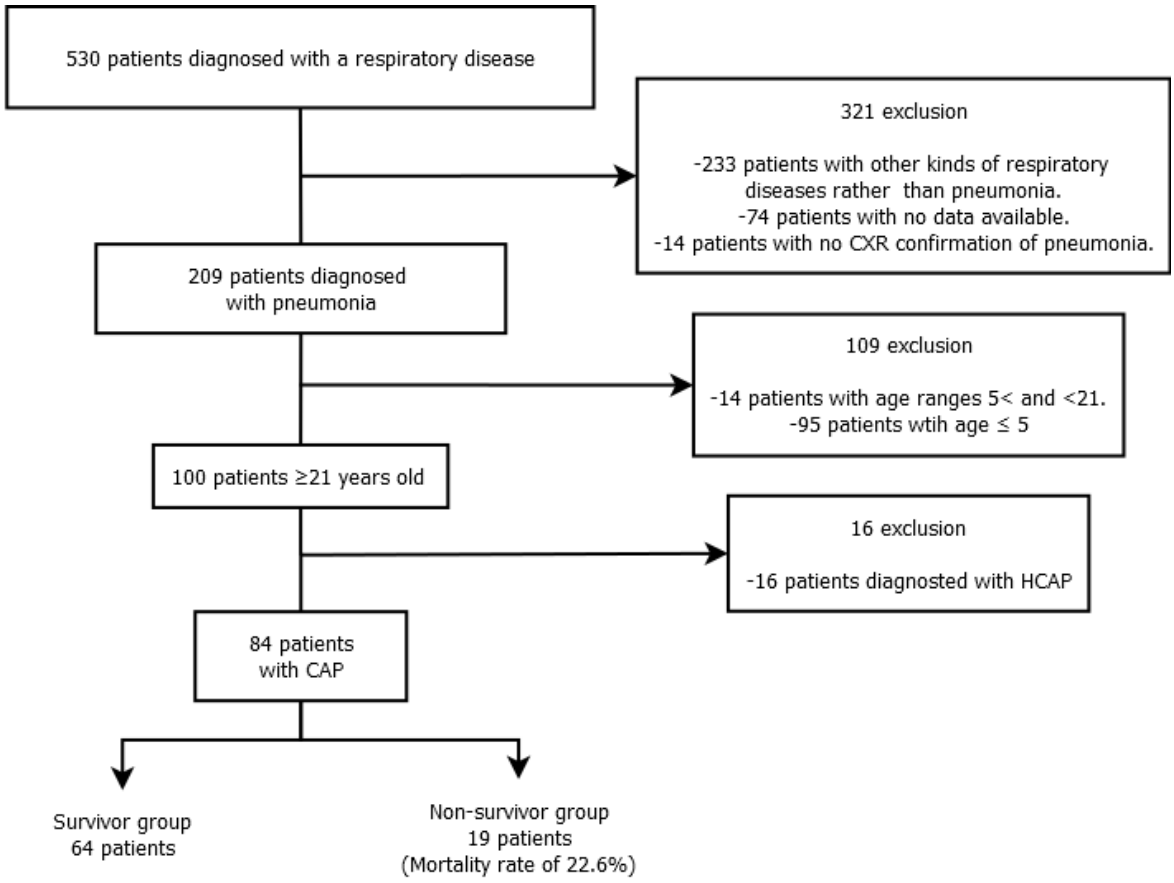
APPENDICES

Appendix A: Complementary information

Figure 5. Patient exclusion diagram.



Other respiratory diseases encompass acute bronchiolitis, chronic obstructive lung diseases, chronic bronchitis simple and mucopurulent, acute pharyngitis, non-specified acute infection of the lower respiratory tract, pneumonitis due to solids and liquids, influenza, other interstitial lung diseases, acute infections of the upper respiratory tract, chronic respiratory disease originated in the perinatal period, acute tonsillitis and other respiratory disorders. Patients with no data available mean no laboratory exams (hemogram, biochemistry, blood electrolytes, and arterial gasometry).

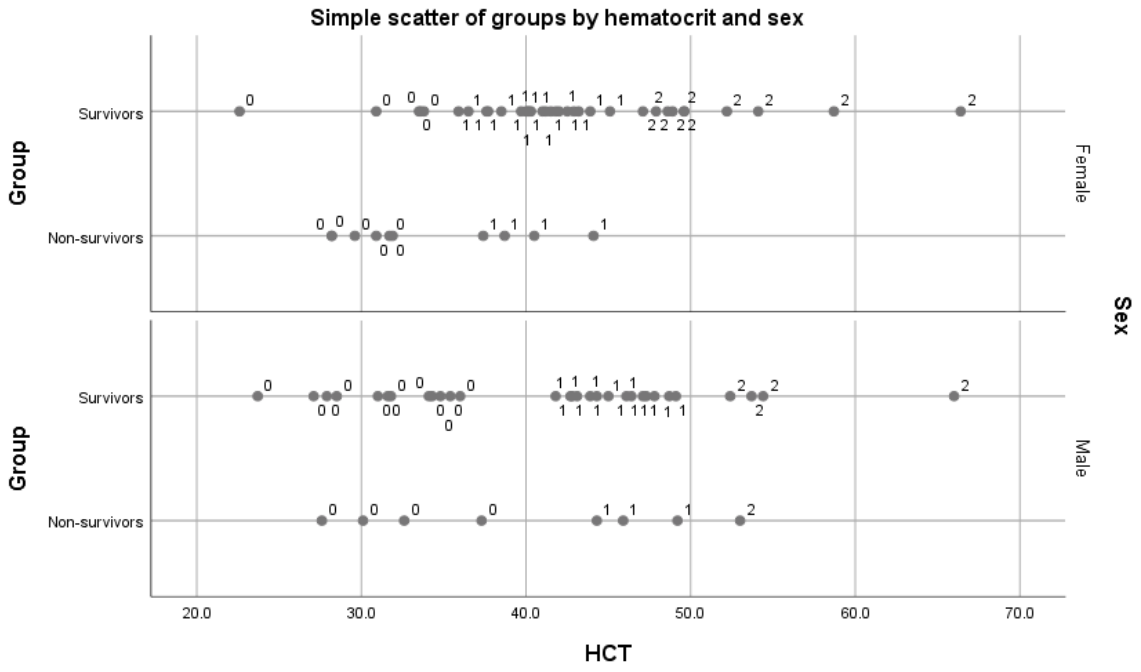
Appendix Table 1. Percentage of missingness of variables

Variable	Missing		Variable	Missing	
	N	Percent		N	Percent
T	14	16.7%	LY pct.	9	10.7%
RR	5	6.0%	NE pct.	6	7.1%
O2sat	7	8.3%	BAS pct.	15	17.9%
			RDW-CV	20	23.8%
WBC	1	1.2%	PDW	25	29.8%
HGB	4	4.8%	Glu	49	58.3%
HCT	1	1.2%	BUN	55	65.5%
MCV	13	15.5%	CR	34	40.5%
MCH	15	17.9%			
MCHC	15	17.9%	Cl	17	20.2%
RDW-SD	23	27.4%	K	17	20.2%
MPV	17	20.2%	Na	17	20.2%
MO	16	19.0%			
EOS	16	19.0%	pH	37	44.0%
LY	16	19.0%	PCO_2	37	44.0%
NE	14	16.7%	PO_2	37	44.0%
BAS	15	17.9%	HCO_3^-	37	44.0%
PLT	3	3.6%	SaO_2	37	44.0%
RBC	12	14.3%	BE	38	45.2%
MO pct.	13	15.5%	BL	39	46.4%
EOS pct.	12	14.3%			

-Frequency and percentage of loss of continuous variables; Complete variables are not showed on the table.

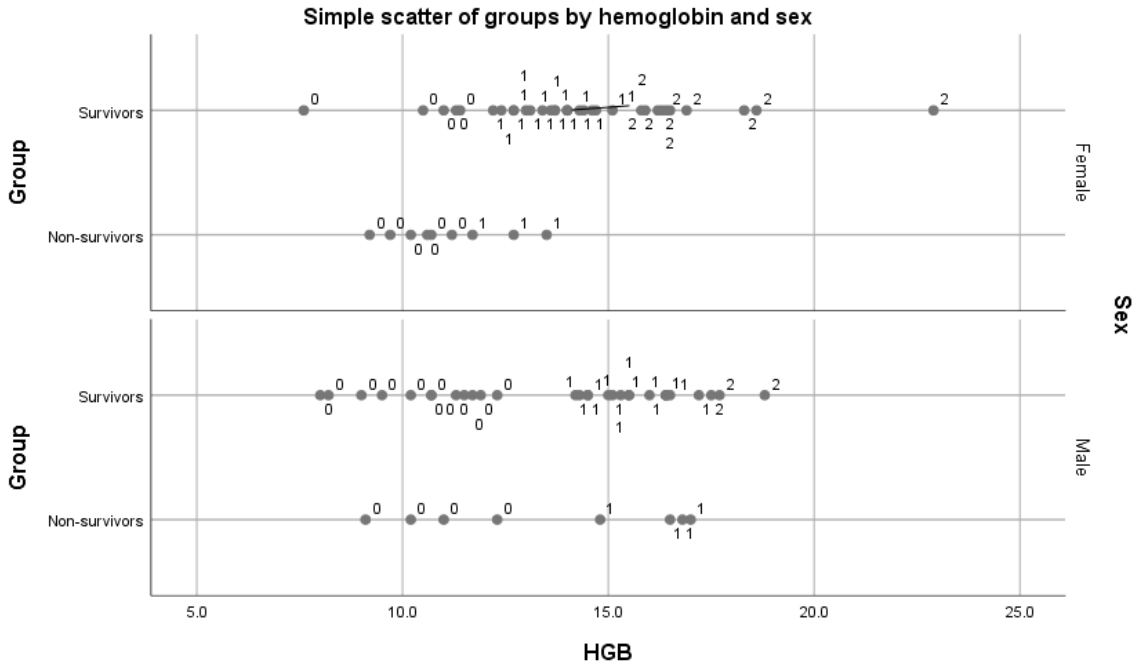
Appendix B: Scatter plots of categorization of variables

Figure 6. Scatter of HCT levels respect to each survival group separated by sex



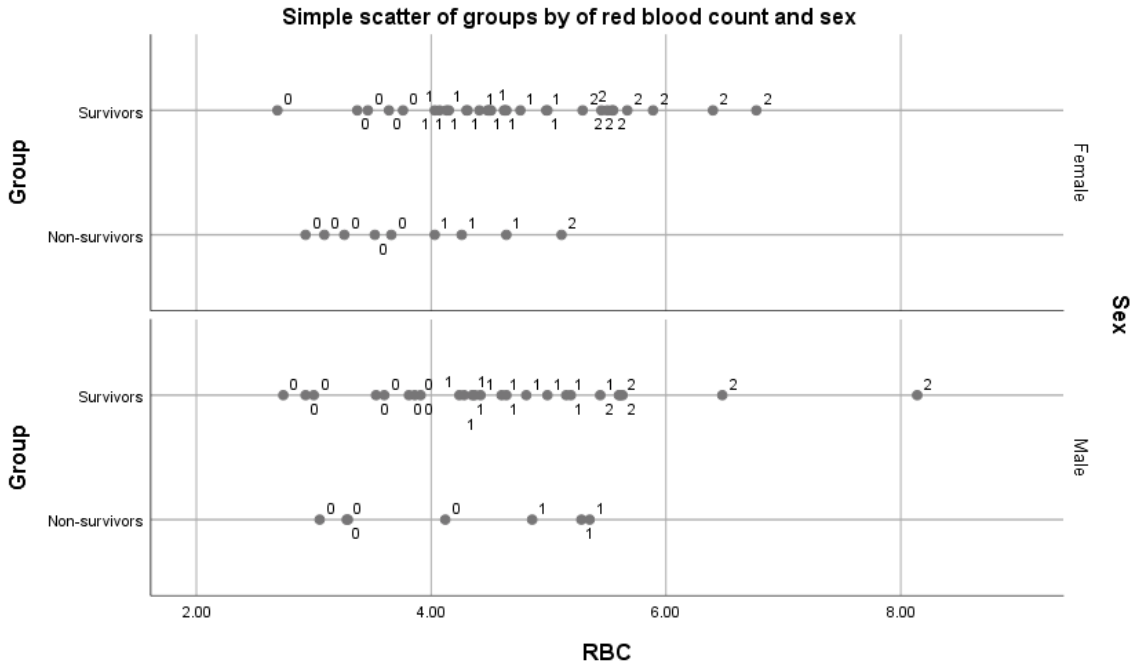
HCT scatter of subgroups of men and women concerning mortality. Levels represented: (0) low, (1) normal, and (2) high. For women, normal levels of HCT are 35 - 45%, and for men are 38 - 51%. Low or high levels are outside the normal reference values. Retrieved from Marshfield Lab.

Figure 7. Scatter of HGB levels respect to each survival group separated by sex.



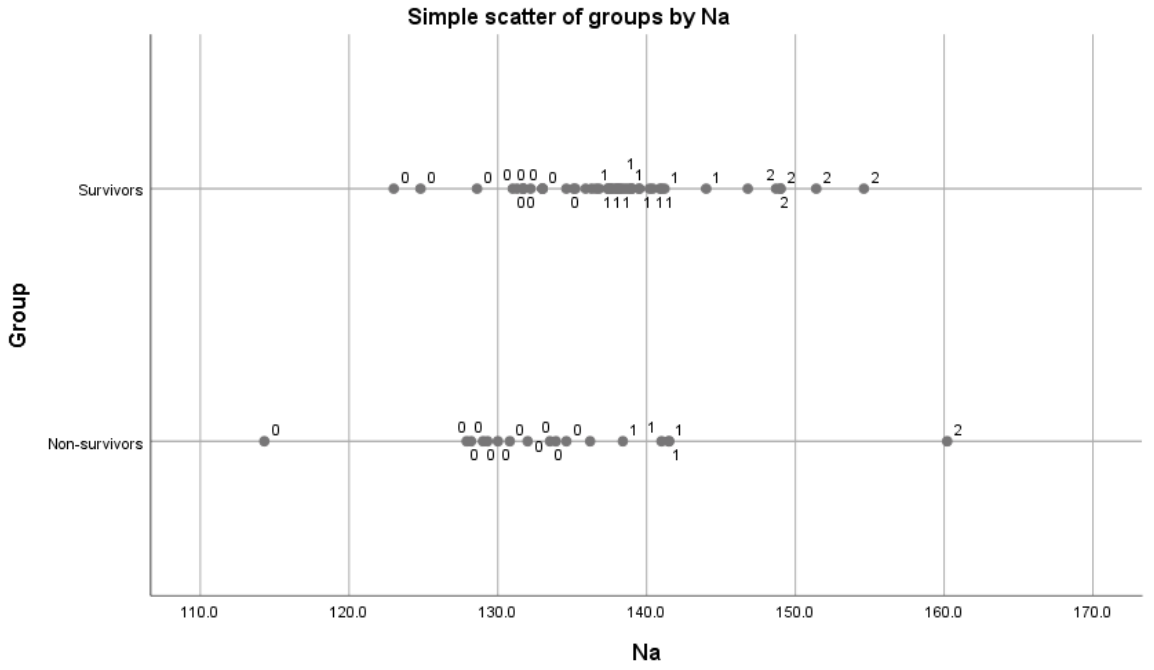
HGB scatter of subgroups of men and women concerning mortality. Levels represented: (0) low, (1) normal, and (2) high. For women normal levels of HGB are 11.7 – 15.5 g / dL and for men are 12.9 – 17.3 g / dL. Low or high levels are outside the normal reference values. Retrieved from Marshfield Lab.

Figure 8. Scatter of RBC levels respect to each survival group separated by sex.



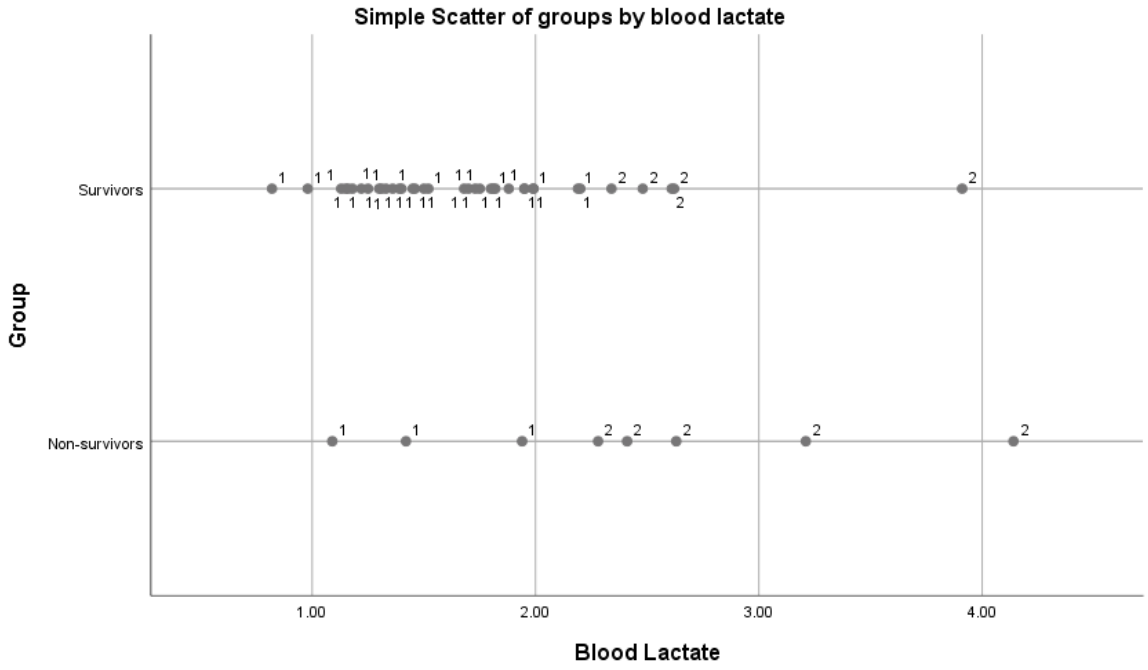
RBC scatter of subgroups of men and women concerning mortality. Levels represented: (0) low, (1) normal, and (2) high. For women, normal RBC levels are 3.85 – 5.05 M / µLa, and men are 4.15 – 5.15 M / µL. Low or high levels are outside the normal reference values. Retrieved from Marshfield Lab.

Figure 9. Scatter of Na levels respect to each survival group.



Sodium scatters of subgroups of men and women concerning mortality. Levels represented: (0) low, (1) normal, and (2) high. No significant differences between men and women: normal sodium levels are: 135 - 147 mEq/L. Low or high levels are outside the normal ranges. Reference values retrieved from CLL Society.

Figure 10. Scatter of blood lactate levels respect to each survival group.



Blood lactate scatters of subgroups of men and women concerning mortality. Levels represented: (1) normal and (2) high. No low levels of BL were detected. No significant differences between men and women, normal levels of BL are 0.5 - 2.2 mmol/L. High levels are outside the normal ranges. Reference values retrieved from MedlinePlus.