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SpO_2/FiO_2 ratio (SF ratio) as a predictor of mortality in ICU patients: Retrospective study using MIMIC Database.

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Capstone Final Report for BSc (Honours) in

Mathematical, Computational and Statistical Sciences

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Chapter 1

Background Information

1.1 Importance of Respiratory Indicators in ICU Studies

Allocation of resources to critical care patients to minimize mortality is a priority for healthcare professionals. As such, the search for connections between various physiological indicators and unfavourable outcomes such as extreme illnesses or even mortality is a constant priority for researchers. This type of research is especially important in the area of healthcare we have chosen to focus on - critical care. A critical care specialist focuses is on the most vulnerable and urgent patients who are placed in an Intensive Care Unit (ICU). There, the specialist keeps track of various physiological indicators to diagnose and treat the patient to maximize their survival. One such important physiological indicator indicator is the PaO_2/FiO_2 ratio (PF ratio), which is used to monitor the patient's pulmonary functions. The numerator, PaO_2 refers to the partial pressure of oxygen in arterial blood and is measured in mmHg via drawing a sample of blood from an artery in the wrist or groin, and testing it in the laboratory. The denominator, FiO_2 refers to the initial fraction

of inspired oxygen and is approximately 21% in breathable atmosphere and can be controlled with the use of mechanical ventilation. The PF ratio is notably used in the diagnosis of extreme illnesses such as Acute Respiratory Distress Syndrome (ARDS) and has been shown to be predictor of mortality in specific subsets of patients such as newborns with Meconium aspiration syndrome (MAS) (Narayanan et al., 2019).

However, there are challenges associated with measurement of PaO_2 specifically. Most importantly, the procedure is invasive and is therefore not easy to measure for all patients and to track at frequent intervals. A more convenient biomarker to measure however is SpO_2 or peripheral capillary oxygen saturation, an estimate of
the amount of oxygen in the blood. It is measured using pulse oximetry, a noninvasive method for monitoring a person's oxygen saturation. Moreover, SpO_2/FiO_2 ratio (SF ratio) has been shown to be a non-invasive surrogate for PaO_2/FiO_2 ratio to diagnose subsets of patients such as children with ALI or ARDS (Rice et al., 2007) and children with smoke inhalation injury (Cambiaso-Daniel et al., 2017).

A retrospective study found that the SpO_2/FiO_2 Time-at-Risk (SF-TAR), defined as the total time spent with severe hypoxemia (SF ratio $\leq$ 145), is not only significantly correlated with hospital mortality for mechanically ventilated patients, but is as well or a better predictor of it than arterial gas-derived measurements of the PF ratio.

Moreover, there have been several studies that aim to link SpO_2 to mortality. In 2015, the Tromsø study concluded that an $SpO_2 \leq 95\%$ is associated by all-cause mortality and mortality caused by pulmonary

diseases (over a 10-year follow-up period) after adjusting for sex, age, history of smoking, self-reported diseases and respiratory symptoms, BMI, and CRP concentration. When Forced Expiratory Volume (FEV1) was included as a covariate, the correlation remained significant for mortality due to pulmonary diseases but no longer significant for all-cause mortality (Vold et al., 2015).

However, a prospectively planned meta-analysis participant data from 5 randomized clinical trials (conducted from 2005-2014) of infants born before 28 weeks' gestation period found no significant difference between a lower SpO_2 target range (85%-89%) and a higher SpO_2 target range (91%-95%) on mortality or major disability at a corrected age of 18 to 24 months (Askie et al., 2018). Therefore, it seems that the use of SpO_2 as a predictor of mortality might not be applicable to all patient phenotypes, with potential for further sub-phenotyping. Such differences between the subpopulation might also be expected for the SF ratio which includes SpO_2 .

1.2 Aim and Objectives

The main goal of this Capstone can be summarized in the following statement:

Investigate whether SpO_2/FiO_2 ratio is a statistically significant predictor of mortality in general ICU patient population or subsets thereof using a retrospective analysis of data.

The use of SpO_2/FiO_2 ratio instead of only SpO_2 allows us to account

for the different levels of mechanical ventilation that an ICU patient receives. In essence, it allows us to account for the patient's ability to convert inspired oxygen to peripheral oxygen saturation at the tissue level.

1.3 Data

For this capstone I will be using **MIMIC III**, an openly available relational database developed by the MIT Lab for Computational Physiology. It contains de-identified data of 61,532 intensive care unit stays: 53,432 stays for adult patients and 8,100 for neonatal patients at the Beth Israel Deaconess Medical Center over the June 2001 - October 2012. It includes demographics, vital signs, laboratory tests, medications, mortality, etc. The database is divided into different tables of data that contain information about a patient's stay and are linked to each via identifiers such as a unique hospital admission ID and a unique patient ID.

Chapter 2

Methods: How to model ICU mortality?

2.1 General Additive Models

2.2 G-Computation

2.3 Pre-Analysis Data Preparation

The pre-analysis data preparation involved extraction of data from different tables, combining them and calculating the SF ratio. The following subsections describe these processes.

2.3.1 Data Extraction

For the patient and stay identifiers I extract SUBJECT_ID, HADM_ID from `ADMISSIONS` table and ICUSTAY_ID from `ICUSTAYS` table. From the `ADMISSIONS` table I extract the time of death of the patient if applicable and if it lies between the ICU admission time and ICU discharge time in `ICUSTAYS` table I indicate ICU mortality. Similarly if the time of death

is between admission time and discharge time in the `ADMISSIONS` table, I indicate Hospital mortality. From the `Patients` table I extract the gender of the patients' and calculate their age.

For all patients and ICU stays I extract the FiO_2 values and their chart times from the `CHARTEVENTS` table. Keeping in mind that at normal atmospheric conditions, FiO_2 is around 21%, I apply the following transformations. For the values between 0 and 1, I convert them to percentages by multiplying by a 100 and only keep those between 21% and 100%. Next, if the reading is recorded as greater than 1 but lower than 21, the value is likely to be erroneous and I discard it. Next, if the value is between 21 and 100, the value is likely to already be a percentage and I take it as such. Finally, I discard all the values above a 100 that are remaining. From the same `CHARTEVENTS` table I extract the patients' height and weight.

From the `CHARTEVENTS` table, I also extract SpO_2 values and chart times but I only keep those which indicate 0 for ERROR which stands for error in measurement. Moreover, I filter the values and I discard those below 10 and above a 100 since they are either physiologically impossible or unlikely.

At the end of this stage, the current dataset accounts for 46,476 Patients, 61,532 ICU Stays with 12,713,362 observations of either SpO_2 or FiO_2 or both. On further examination of the data, I find that for every FiO_2 measurement for a given ICU stay, for a given unique patient, there is a corresponding SpO_2 measurement at the same chart time but not vice versa. Accordingly, I restrict my data to only those chart times with both SpO_2 and FiO_2 measurements. This further subsets the number of observations further into 703,201 observations.

Chapter 3

Covariates

3.1 Covariate Selection

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3.1.1 To Ratio or not to Ratio

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3.1.2 Does Transformation help?

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3.2 Timeframe of SF Ratio aggregation

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Appendix A

Other Figures

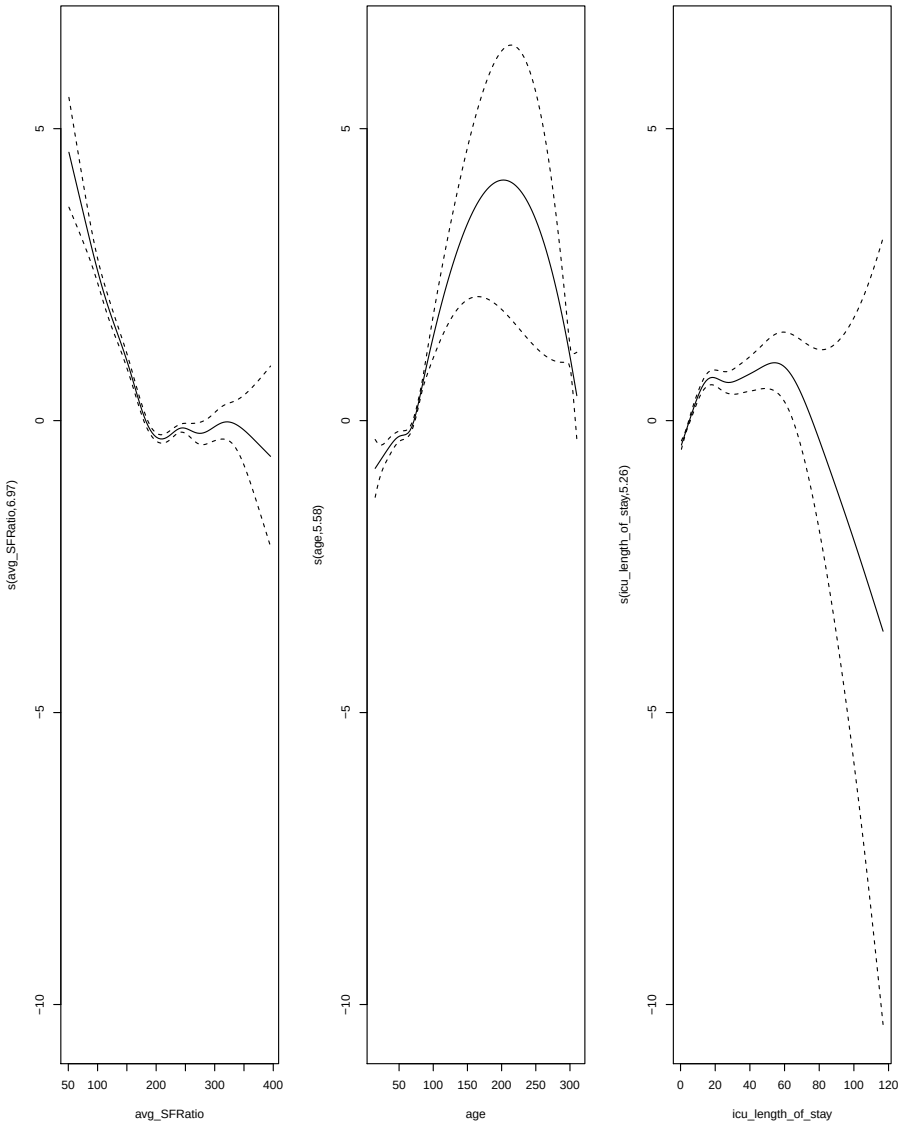

FIGURE A.1: Results of GAM model