**Measurements and results(Abstract)­**

**Methods**

We retrospectively tested the changes in CVP and DBP with hypoxemia in MIMIC-III (Medical Information Mart for Intensive Care III) database. Hypoxemia was defined according to oxygenation index(OI < 100 as severe, OI <200 as moderate). The primary outcomes were the mean CVP and mean DBP measurements 6 hours after the onset of hypoxemia comparing with that 6 hours before the event.

**Results**

According to the definition of hypoxemia, 615 patients met criteria for severe hypoxemia, 1301 patients met criteria for moderate hypoxemia. The results showed CVP increased significantly in the following 6 hours for severe hypoxemia patients. However there is no evidence showing a significant change in DBP for both severe and moderate hypoxemia patients.

**Methods**

**MIMIC-III database**

We conducted a retrospective study on the Medical Information Mart for Intensive Care’ database(MIMIC-III)[1]. MIMIC is a large open access database comprising high temporal resolution data including vital signs, medications, laboratory measurements, observations and electronic documentations for all patients admitted to Beth Israel Deaconess Medical Center (BIDMC) ICUs between 2001 and 2012[2].

**Study population**

We extracted all patients with hypoxemia in MIMIC-III database, where hypoxemia was defined according to oxygenation index, the ratio of partial pressure of arterial oxygen and fraction of inspired oxygen, we proposed two severity degrees of hypoxemia: severe and moderate[3]. The observation window for pre- and post- hypoxemia was 6 hours ahead and 6 hours afterwards onset time correspondingly.

Among all 46520 MIMIC patients, 4648 patients were identified as severe hypoxemia during their stay. We excluded 623 patients having mechanical ventilation treatment records during their stay, 2316 used vasopressor in 6 hours, 1094 records with missing value were leaved out. Finally 615 unique admissions records were included into cohort. For moderate hypoxemia, 1301 unique admissions met the criteria of OI < 200 that without vasopressor nor mechanical ventilation records.

**Study outcomes**

The primary outcomes were mean central venous pressure(CVP) and mean diastolic blood pressure(DBP) measured 6 hours after the onset of hypoxemia and 6 hours before the onset event.

**Confounding factor control**

Values of heart rate and PEEP were collected from MIMIC database. Mean value of heart rate and PEEP were calculated in 6 hours before hypoxemia onset and 6 hours after the event.

**Statistical analyses**

Data are summarized using median and interquartile ranges(IQRs). The Kolmogorov-Smirnov test was used to examined the normality of continuous variables. And Kruskal-Wallis test was employed to determine the significance among non-normal continuous variables.

To compare outcome variables (CVP and DBP) pre- and post- the onset of, we developed multivariable linear regression models that adjusted the effect of PEEP and heart rate. The categories of whether vital signs were measured before or after hypoxemia was included as categorical variable. CVP, DBP, PEEP and heart rate were included as continuous variables. The analysis using package glm in R.

The data extraction was performed using pgAdmin4 and all statistical analyses were performed with customized scripts using R 3.4.3.

**Results**

The variable characteristics of the two population were summarized in **Table 1**. For severe hypoxemia patients, median CVP measured before and after hypoxemia were 14(IQR, 10.82-18) and 14.48(IQR, 11.5-18.89) respectively. Kruskal-Wallis test showed a significant difference in CVP(p = 0.028) and PEEP(p < 0.001).

Results of multivariable linear regression model for severe hypoxemia patients were shown in **Table 2** and **Table 3.** In Table 2, model for CVP showed a significant change in CVP (p = 0.015) after adjusting for PEEP and heart rate. While in Table 3, the result indicated no significant difference in DBP before and after hypoxemia. **Table 4** and **Table 5** showed results for moderate hypoxemia patients that indicated no significant difference in CVP and DBP.

**Table 1. variable characteristics of hypoxemia patients**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Severe hypoxemia patients（n = 615） | | | Moderate hypoxemia patients（n = 1301） | | |
|  | pre | post | P value | pre | post | P value |
| CVP (median [IQR]) | 14.00  [10.82, 18.00] | 14.48  [11.50, 18.89] | 0.028 | 13.00  [10.00, 16.67] | 13.23  [10.11, 16.80] | 0.417 |
| DBP (median [IQR]) | 56.20  [49.62, 62.52] | 56.39  [49.51, 63.18] | 0.669 | 56.28  [50.47, 62.88] | 56.33  [50.50, 62.42] | 0.991 |
| PEEP (median [IQR]) | 7.67  [5.00, 10.00] | 8.33  [5.00, 12.00] | <0.001 | 5.00  [5.00, 8.75] | 6.50  [5.00, 10.00] | <0.001 |
| Heart rate  (median [IQR]) | 95.67  [81.73, 109.42] | 94.67  [81.50, 107.29] | 0.356 | 89.98  [78.81, 103.17] | 89.17  [79.03, 102.50] | 0.468 |

**Table 2. Multivariable linear regression model of CVP in severe hypoxemia patients, adjusted for PEEP and heartrate**

|  |  |  |
| --- | --- | --- |
|  | Coef(95% CI) | P value |
| CVP measured Pre or Post | 3.63(0.70, 6.56) | 0.015 |
| PEEP | 0.33(-0.02, 0.67) | 0.063 |
| Heart rate | 0.05(-0.03, 0.13) | 0.202 |

**Table 3. Multivariable linear regression model of DBP in severe hypoxemia patients, adjusted for PEEP and heartrate**

|  |  |  |
| --- | --- | --- |
|  | Coef(95% CI) | P value |
| DBP measured Pre or Post | 0.32(-0.87, 1.51) | 0.597 |
| PEEP | 0.07(-0.07, 0.21) | 0.314 |
| Heart rate | 0.10(0.06, 0.13) | <0.001 |

**Table 4. Multivariable linear regression model of CVP in moderate hypoxemia patients, adjusted for PEEP and heartrate**

|  |  |  |
| --- | --- | --- |
|  | Coef(95% CI) | P value |
| CVP measured Pre or Post | 1.58 ( -0.01 , 3.18 ) | 0.05 |
| PEEP | 0.42 ( 0.18 , 0.67 ) | 0.001 |
| Heart rate | 0.11 ( 0.07 , 0.16 ) | < 0.001 |

**Table 5. Multivariable linear regression model of DBP in moderate hypoxemia patients, adjusted for PEEP and heartrate**

|  |  |  |
| --- | --- | --- |
|  | Coef(95% CI) | P value |
| DBP measured Pre or Post | -0.08 ( -0.84 , 0.69 ) | 0.844 |
| PEEP | 0.12 ( 0 , 0.24 ) | 0.041 |
| Heart rate | 0.09 ( 0.07 , 0.11 ) | <0.001 |

1. MIMIC-III, a freely accessible critical care database. Johnson AEW, Pollard TJ, Shen L, Lehman L, Feng M, Ghassemi M, Moody B, Szolovits P, Celi LA, and Mark RG. Scientific Data (2016). DOI: [10.1038/sdata.2016.35](http://dx.doi.org/10.1038/sdata.2016.35). Available at: <http://www.nature.com/articles/sdata201635>
2. Pollard, T. J. & Johnson, A. E. W. The MIMIC-III Clinical Database <http://dx.doi.org/10.13026/C2XW26> (2016)
3. Ferguson N D, Fan E, Camporota L, et al. The Berlin definition of ARDS[J]. Intensive Care Medicine, 2012, 38(10):1573.