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# Respiratory Parameters and Arterial Blood Gases Test as Predictors of Extubation Failure in Preterm Infant

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## ABSTRACT

**Background:** The preterm survival is increased by mechanical ventilation but its prolonged unnecessary utilization results in certain complications. Therefore, if the infant is "ready for extubation," extubation should be performed immediately. However, a failed extubation during reintubation attempts may also cause complications. There are no standard recommendations and predictors for the safe extubation of preterm neonates at present. **Objective:** The aim of the current study was to evaluate respiratory severity scores (tidal volume paco2, O2 saturation) for prediction of extubation failure.

**Patients and methods:** A prospective cohort study was conducted on 40 preterm mechanically ventilated infants in Neonatal Intensive Care Unit (NICU), Faculty of Medicine, Zagazig University Children Hospitals. All recruited preterm infants were of <35 weeks gestational age and were ready for extubation. All patients underwent measurement of arterial blood gases respiratory parameters. **Results:** After using ROC curve, oxygenation index, RSS, RSS/kg and $PO_2$ were found to be good predictors for failed extubation.

**Conclusion:** In pre-term infant**,** $O_2$ saturation, $Paco_2$, Tidal volume, Respiratory severity score showed high sensitivity and specificity for extubation failure prediction.

**Keywords:** Preterm, Extubation failure, Arterial blood gases, Cohort study, Zagazig University.

## INTRODUCTION

Respiratory distress syndrome (RDS) is the leading cause of early newborn mortality and long-term consequences. Due to immature lung development, surfactant deficiency, and other organs immaturity, these neonates have RDS and respiratory failure. Numerous infants with RDS continue to develop chronic lung disease (CLD) and are at high risk for ongoing respiratory morbidity throughout childhood and adulthood **[1,2]**.

When preterm neonates are born with inadequate pulmonary surfactant, they undergo respiratory distress characterized by rapid, labored breathing, grunting, and central cyanosis. During the first few days after delivery, respiratory distress frequently worsens as the airways gradually collapse as a result of an increase in surface tension. If a newborn survives the initial few days, the lungs begin producing surfactant, respiratory distress stabilizes, and then diminishes as the lungs reinflate. Supplemental oxygen was the only effective treatment for RDS **[3]**.

In spite of the fact that non-invasive techniques for respiratory care of preterm infants with very low birth weight (VLBW) have grown in popularity and are employed more frequently in recent years, a considerable proportion of these infants still require mechanical ventilation (MV) **[4]**.

Despite their lifesaving potential, endotracheal intubation and MV are associated with bacterial colonization, sepsis, ventilator-related pneumonia, and airway damage **[5]**.

Nowadays, extubation decisions are typically reliant on subjective clinical assessments influenced by ventilator parameters, blood gas levels, and interpretation of the infant's clinical status; this may result in incorrect extubation **[6]**.

Extubation failure is associated not only with prolonged MV time, but also with increased mortality and longer hospital stays **[7]**.

Bradycardia, blood pressure variations, hypoxemia and cerebral function alterations may be caused by recurrent endotracheal intubation and complications (as atelectasis and upper airway injuries) are potential causes of these adverse outcomes **[8]**.

The respiratory severity score (RSS) is a non-invasive, blood sample-free method for respiratory failure evaluation. In numerous large multicenter investigations, it has been utilized as a marker of illness severity. Additionally, its association with short-term complications, BPD & mortality has been studied and high RSS readings have been linked to extubation failure **[9,10]**.

Furthermore, researchers are evaluating clinical and physiological data throughout a predetermined period of time without mechanical inflations, either by briefly disconnecting the ventilator or by using endotracheal continuous positive airway pressure (ETT-CPAP). Diverse extubation readiness tests, such as spontaneous breathing trials (SBT), have been included into clinical practice around the world; however their utility has not been shown **[6]**.



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According to retrospective investigations of extubation preparedness and extubation failure in preterm newborns, extubation failure is associated with a lower birthweight, a lower GA, inadequate lung expansion on chest X-ray, and a higher fraction of inspired oxygen ($FiO_2$) prior to extubation [11,12]. Historically, the timing of extubation was largely determined by clinicians based on variables such as GA, postnatal age, weight, $FiO_2$ or spontaneous breathing tests [13].

Infants with extubation failure had higher pre- and post-extubation $FiO_2$ values [14].

**Fernandes *et al.*** [15] confirms that there is a higher risk of failure in mechanically ventilated infants and children when there is decreased central inspiratory drive as indicated by a low Vt/Ti, when the effort of breathing leading to a lower-than-normal spontaneous tidal volume, or when there is an increased load on the respiratory muscles as indicated by a high PIP or a low dynamic compliance.

The aim of the current study was to evaluate respiratory severity scores (tidal volume paco2, O2 saturation) for prediction of extubation failure.

## PATIENTS AND METHODS

A prospective cohort study was conducted on 40 preterm mechanically ventilated infants in Neonatal Intensive Care Unit (NICU), Faculty of Medicine, Zagazig University Children Hospitals, between November 2022 and April 2023.

All recruited preterm infants were <35 weeks gestational age and were ready for extubation. There were 21 males and 19 females. Their birth weight ranged from 1.2-2.5 kg. The study comprised infants <35 weeks of GA who were intubated for respiratory failure on the first postnatal day and had their first planned extubation. Exclusion criteria for the study were infants >35 weeks gestation, late transfer after the first postnatal day, the presence of a major congenital abnormality, unplanned extubation and infants who died or were transferred without extubation.

All patients underwent a comprehensive history gathering that involved perinatal and birth data. The settings for the mechanical ventilator one hour previous to the initial extubation were collected from nursing and medical records, including mean airway pressure (MAP), positive end expiratory pressure, tidal volumes (VT): set by clinicians (set Vt) and measured by the infant (measured Vt), $FiO_2$, peak inspiratory pressure (set for infants receiving pressure-limited ventilation and measured for those receiving volume-targeted ventilation), RSS and oxygenation index. Blood gases were analyzed. The settings for non-invasive respiratory support were recorded immediately after extubation. After extubation, patients were monitored for 48 hours and the extubation success or failure was recorded. If extubation was unsuccessful, the parameters were modified. From the clinical notes, the reasons for re-intubation and the problems of re-intubation were extracted. Infants could have more than one reason for re-intubation, such as a rising $FiO_2$ need or respiratory acidosis, apnea, hypercapnia, or upper airway blockage. The extubation time and patients' weight who undergoing scheduled extubation were documented. RSS and RSS/kg values were estimated before to extubation. Using the following formula, RSS was estimated:

$$\mathbf{RSS: MAP \times FiO2}$$

MAP: mean airway pressure; $FiO_2$ (inspired oxygen fraction) Where $FiO_2$ expressed by fraction.

During the first 2 postnatal weeks, the patient's birth weight was utilized to estimate **RSS/kg**, while the current weight was used on subsequent days.

**Pre-extubation OI** was estimated. The following formula was used to estimate OI:

$$OI = \frac{MAP \times FiO_2 \times 100}{PaO_2}$$

Where $FiO_2$ expressed by fraction

**Extubation:**

The optimal time to extubate a premature newborn is not clear. Thus, prior to the commencement of the trial, we established the following criteria for determining when a patient is "ready" for extubation:

For infants ≥1000 g: FiO2 ≤ 0.3 & MAP ≤8 cmH2O.

For infants<1000 g: FiO2 ≤ 0.3 & MAP ≤ 7 cmH2O.

Nonetheless, the responsible physician makes all decisions about weaning, extubation readiness evaluation, and post-extubation treatment. Generally, all units have chosen $SpO_2$ goal ranges in accordance with their particular institutional instruction and have been employing a hypercapnia-permissive ventilator strategy. Since the conception of the study and the initiation of patient enrollment, we have witnessed an increase in the number of newborns extubated to CPAP.

**Extubation failure in the first 48 h after extubation:**

Presence of one or more of the following criteria was utilized to define the extubation failure:

- One apnea episode requiring bag and mask breathing with positive pressure ventilation.
- Multiple apnea episodes (≥6 episodes/6 hours).
- $PaCO_2$ >55-60 mmHg with a pH <7.25, in two consecutive blood gases done at least 1 hour apart.
- $FiO_2$ >0.5 to maintain $SpO_2$ > 88% or $PaO_2$ >45 mmHg (for 2 consecutive hours).
- This data was gathered prospectively using blood gas records and the nursing flow chart.

**Extubation failure after 48 hours of extubation:**

After 48 hours of extubation, neonates were observed for the existence of extubation failure criteria.

**Reintubation:**
It was documented at any moment between extubation and NICU discharge. Since the responsible physician took the decision to re-intubate, the timing and reasons for reintubation were meticulously documented. Consequently, the reintubation indications were distinct from the criteria indicating extubation failure.

**Ethical Consideration:**
**This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University (ZU-IRB 9820/20-9-2022). Written informed consent was obtained from all parents or guardians. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.**

***Statistical Analysis***
The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp. Released 2019) version 26 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher's exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as mean and standard deviation (SD), and independent sample t-test/Mann-Whitney test was used for comparison between groups. In order to find the optimal cutoff value for a quantitative parameter utilized in the diagnosis of a health concern, the ROC curve was analyzed. Risk variables for a health condition were separated out using binary logistic regression. P value ≤0.05 was considered to be statistically significant.

**RESULTS**
As shown in table 1, there is **a significant** relation between outcome and GA & birth weight. Infants with failed extubation had significantly lower GA and birth weight. There is an **insignificant** relation between outcome and either mode of delivery and sex.

**Table (1):** Relation between extubation outcome and neonatal risk factors:

| Variable | Failure N=21 (%) | Success N=19 (%) | $\chi^2$ | P-value |
|---|---|---|---|---|
| **Sex:** | | | | |
| Female | 9 (42.9%) | 10 (52.6%) | 0.382 | 0.536 |
| Male | 12 (57.1%) | 9 (47.4%) | | |
| **Mode of delivery:** | | | | |
| NVD | 15 (71.4%) | 15 (78.9%) | Fisher | 0.721 |
| CS | 6 (28.6%) | 4 (21.1%) | | |
| | **Mean ± SD** | **Mean ± SD** | **t-test** | **P-value** |
| **Gestational age (week)** | 31.24 ± 2.19 | 33.84 ± 1.43 | -4.5 | **<0.001**** |
| **Birth weight (kg)** | 1.567 ± 0.3 | 2.107 ± 0.291 | -5.749 | **<0.001**** |

t independent sample t test, **P≤0.001 is statistically highly significant, $\chi^2$: Chi square test.

As shown in **table 2**, there is a **significant** relation between outcome and use of antenatal steroids (significantly related with extubation success). There is **insignificant** relation between outcome and maternal risk factors.

**Table (2):** Relation between extubation outcome and maternal risk and medications

| Variable | Failure N=21 (%) | Success N=19 (%) | t-test | P-value |
|---|---|---|---|---|
| **Maternal risk factor:** | | | | |
| PROM | 8 (38.1%) | 2 (10.5%) | Fisher | 0.069 |
| Chorioamnionitis | 3 (14.3%) | 0 (0%) | Fisher | 0.233 |
| Diabetes | 0 (0%) | 1 (5.3%) | Fisher | 0.475 |
| Incompetent cervix | 2 (9.5%) | 0 (0%) | Fisher | 0.489 |
| Multiple pregnancy | 8 (38.1%) | 2 (10.5%) | Fisher | 0.069 |
| Placenta previa | 0 (0%) | 2 (10.5%) | Fisher | 0.219 |
| Accidental vaginal bleeding | 2 (9.5%) | 0 (0%) | Fisher | 0.489 |
| **Antenatal steroid** | 9 (42.9%) | 16 (84.2%) | 7.278 | **0.007*** |

*P<0.05 is statistically significant. $\chi^2$: Chi square test.

As shown in **table 3**, there is a **significant** relation between outcome and cardiac lesions, Down score (higher scores associated with failure), duration of pre-intubation support (significantly lower in patients with failure) and size and length of tube (significantly lower in patients with failure). There is **insignificant** relation between outcome and presence of sepsis, HMD, MAS, congenital pneumonia, intractable apnea, pulmonary hypertension, need for respiratory support, age at intubation or receiving Surfactant.

**Table (3):** Relation between extubation outcome and diagnosis.

| Variable | Failure N=21 (%) | Success N=19 (%) | t-test | P-value |
|---|---|---|---|---|
| **Pulmonary hypertension** | 2 (9.5%) | 2 (10.5%) | Fisher | >0.999 |
| **Sepsis** | 4 (19%) | 0 (0%) | Fisher | 0.108 |
| **Intractable apnea** | 2 (9.5%) | 0 (0%) | Fisher | 0.488 |
| **HMD** | 14 (66.7%) | 8 (42.1%) | 2.431 | 0.119 |
| **MAS** | 0 (0%) | 2 (10.5%) | Fisher | 0.219 |
| **Congenital pneumonia** | 25 (23.8%) | 2 (10.5%) | Fisher | 0.412 |
| **Cardiac anomalies** | | | MC | <0.001** |
| Absent | 17 (81%) | 6 (31.6%) | | |
| PDA | 4 (19%) | 10 (52.6%) | | |
| VSD, PDA | 0 (0%) | 3 (15.8%) | | |
| **Down score** | | | 3.882¥ | **0.049*** |
| **5** | 2 (9.5%) | 6 (31.6%) | | |
| **6** | 4 (19%) | 6 (31.6%) | | |
| **7** | 10 (47.6%) | 4 (21.1%) | | |
| **8** | 5 (23.8%) | 3 (15.8%) | | |
| **Respiratory support** | | | 0.819 | 0.366 |
| Absent | 7 (33.3%) | 9 (47.4%) | | |
| Present | 14 (66.7%) | 10 (52.6%) | | |
| **Age at intubation:** | | | 0.819 | 0.366 |
| First day | 14 (66.7%) | 10 (52.6%) | | |
| First hour | 7 (33.3%) | 9 (47.4%) | | |
| **Receiving surfanta** | 17 (81%) | 10 (52.6%) | 3.647 | 0.056 |
| **Duration of pre-intubation support (hours)** | **Median (IQR)** | **Median (IQR)** | **Z** | **p** |
| | 6(3 – 12) | 12(5.25 – 24) | -4.799 | **<0.001**** |
| **Size of tube (Cm)** | **Mean ± SD** | **Mean ± SD** | **t** | **p** |
| | 2.83 ± 0.24 | 3 ± 0 | -3.162 | **0.005*** |
| **Length of tube (Cm)** | 8.5 ± 0.32 | 8.79 ± 0.25 | -3.171 | **0.003*** |

*P<0.05 is statistically significant. $\chi^2$: Chi square test. ¥Chi square for trend test. **P≤0.001 is statistically highly significant.

As shown in **table 4**, within each group, there is a significant drop in PIP, PEEP, $FiO_2$, and MAP one hour prior to extubation, than baseline values. There is a **significant** relation between outcome and all of mode of MV, FiO2, and MAP baseline and 1 hour before extubation (were **significantly** higher among patients with failed extubation both baseline and 1 hour before extubation). There is **insignificant** relation between outcome and all of type of MV, duration of first intubation, and PEEP, PIP baseline and 1 hour before extubation.

**Table (4):** Relation between extubation outcome and different parameters.

| Variable | Failure (n=21) | Success (n=19) | t-test | P-value |
|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | |
| **PEEP baseline** | 6.3 ± 0.64 | 6.42 ± 0.69 | -0.597 | 0.554 |
| **PEEP before extubation** | 5.5 ± 0.51 | 5.32 ± 0.63 | 0.994 | 0.327 |
| **Pt** | **<0.001**** | **<0.001**** | | |
| **PIP baseline** | 19.43 ± 1.89 | 18.42 ± 1.77 | 1.735 | 0.091 |
| **PIP before extubation** | 12.76 ± 1.0 | 12.32 ± 0.7 | 1.611 | 0.116 |
| **Pt** | **<0.001**** | **<0.001**** | | |
| **FiO2 baseline** | 77.14 ± 6.24 | 58.42 ± 4.73 | 10.606 | **<0.001**** |
| **FiO2 before extubation** | 36.9 ± 3.35 | 29.21 ± 3.82 | 6.788 | **<0.001**** |
| **Pt** | **<0.001**** | **<0.001**** | | |
| **Mean airway pressure baseline** | 12.32 ± 0.81 | 11.33 ± 1.06 | 3.351 | **0.002*** |
| **MAP before extubation** | 8.71 ± 0.5 | 8.17 ± 0.5 | 3.44 | **<0.001**** |
| **Pt** | **<0.001**** | **<0.001**** | | |
| | **N=21 (%)** | **N=19 (%)** | **$\chi^2$** | **P-value** |
| **Type of MV:**<br>Drager baby log **800**<br>**SLE 5000** | 19 (90.5%)<br>2 (9.5%) | 17 (89.5%)<br>2 (10.5%) | Fisher | >0.999 |
| **Mode:**<br>**A/C, ptv, sippv**<br>**SIMV** | 2 (9.5%)<br>19 (90.5%) | 10(52.6%)<br>9 (47.4%) | Fisher | 0.007* |
| | **Median (IQR)** | **Median (IQR)** | Z | P-value |
| **Duration of first intubation (days)** | 12(11 – 13) | 7(6.75 – 8.75) | -1.337 | 0.181 |

*P<0.05 is statistically significant. **$\chi^2$:** Chi square test. **P≤0.001 is statistically highly significant, **Z:** Mann Whitney test. **IQR:** interquartile range, P**t:** Paired sample t test.

As shown in **table 5**, there is a **significant** relation between outcome and $PO_2$ baseline and 1 hour before extubation ($PO_2$ was **significantly** lower in failed extubation both baseline and 1 hour before extubation). There is an **insignificant** relation between outcome and either $HCO_3$, $PaCO_2$ or PH baseline and 1 hour before extubation. There is a considerable drop in PH, $PaCO_2$, and $PO_2$ within each group 1 hour before extubation compared to baseline readings. Within patients with a poor outcome, there is a substantial increase in $HCO_3$ one hour prior to extubation, whereas there is an insignificant increase in $HCO_3$ among groups with successful extubation.

**Table (5):** Relation between extubation outcome and ABG baseline and 1 hour before extubation.

| Variable | Failure (n=21) | Success (n=19) | t-test | P-value |
|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | |
| **PH baseline** | 7.19 ± 0.05 | 7.23 ± 0.12 | -1.326 | 0.198 |
| **PH before extubation** | 7.4 ± 0.03 | 7.39 ± 0.04 | 1.085 | 0.287 |
| **Pt** | **<0.001**** | **<0.001**** | --- | |
| **PaCO2 baseline** | 58.38 ± 6.84 | 56.0 ± 11.49 | 0.805 | 0.426 |
| **PaCO2 before extubation** | 37.52 ± 1.57 | 37.53 ± 2.97 | -0.003 | 0.997 |
| **Pt** | **<0.001**** | **<0.001**** | --- | |
| **HCO3 baseline** | 20.46 ± 4.21 | 22.91 ± 4.96 | -1.685 | 0.1 |
| **HCO3 before extubation** | 22.65 ± 2.12 | 22.43 ± 3.06 | 0.257 | 0.799 |
| **Pt** | **0.035*** | 0.768 | --- | |
| **PO2 baseline** | 35.9 ± 7.11 | 47.89 ± 9.6 | -4.053 | **<0.001**** |
| **PO2 before extubation** | 64.92 ± 6.43 | 93.41 ± 11.05 | -10.087 | **<0.001**** |
| **Pt** | **<0.001**** | **<0.001**** | --- | |

*P<0.05 is statistically significant. **P≤0.001 is statistically highly significant. **Pt:** Paired sample t test.

As shown in **table 6**, there is a **significant** relation between outcome and RSS and RSS/kg baseline and 1 hour before extubation (RSS and RSS/kg baseline and 1 hour before extubation were **significantly** higher among patients with failed extubation both baseline and 1 hour before extubation). Within each group, there is significant decrease in RSS and RSS/kg 1 hour before extubation as compared to baseline values. There is a **significant** relation between outcome and oxygenation index baseline and 1 hour before extubation (oxygenation index was **significantly** higher among patients with failed extubation both baseline and 1 hour before extubation). Within each group, there is significant decrease in oxygenation index 1 hour before extubation as compared to baseline values.

**Table (6):** Relation between outcome of extubation and RSS, RSS/kg baseline (at intubation) and 1 hour before extubation, oxygenation index baseline and before extubation.

| Variable | Failure (n=21) | Success (n=19) | t-test | P-value |
|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | |
| **RSS baseline** | 9.08 ± 1.35 | 6.88 ± 1.11 | 5.568 | <0.001** |
| **RSS before extubation** | 3.04 ± 0.62 | 2.48 ± 0.47 | 3.212 | <0.001** |
| **pt** | **<0.001**** | **<0.001**** | --- | |
| **RSS/kg baseline** | 5.97 ± 1.31 | 3.32 ± 0.71. | 8.017 | <0.001** |
| **RSS/kg before extubation** | 1.98 ± 0.45 | 1.21 ± 0.33 | 6.214 | <0.001** |
| **pt** | **<0.001**** | **<0.001**** | | |
| **Oxygenation index baseline** | 34.75 ± 7.87 | 21.66± 5.34 | 4.503 | <0.001** |
| **Oxygenation index before extubation** | 6.21 ± 1.5 | 3.83 ± 0.7 | 5.839 | <0.001** |
| **Pt** | **<0.001**** | **<0.001**** | --- | |

*P<0.05 is statistically significant. **P≤0.001 is statistically highly significant. Pt Paired sample t test.

Lower weight at extubation, higher oxygenation index, and increase RD, while higher birth weight and gestational age, decrease risk of extubation failure. On the other hand, higher down score, non-use of antenatal steroid and higher baseline RSS and HMD increase risk of failure by 3.62, 3.586, 1.199 and 169.42 folds, respectively (**Table 7**).

**Table (7):** Multivariate regression analysis of factors associated with failure of extubation among studied patients.

| Variable | β | P-value | AOR | 95% C.I. | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| **Low GA(week)** | 0.079 | 0.772 | 2.924 | 0.542 | 4.576 |
| **Low Birth weight (kg)** | 0.127 | 0.345 | 1.135 | 0.872 | 1.477 |
| **Low use of Antenatal steroid** | **1.533** | **0.017*** | **3.704** | **1.783** | **9.707** |
| **High Cardiac anomalies** | 0.122 | 0.668 | 1.885 | 0.506 | 3.548 |
| **High Down score** | **1.268** | **0.002*** | **6.281** | **1.124** | **10.64** |
| **Low Duration of pre-intubation support (hours)** | 0.102 | 0.652 | 1.108 | 0.710 | 1.730 |
| **Low Size of tube (Cm)** | 0.079 | 0.772 | 1.135 | 0.872 | 2.477 |
| **Low Length of tube (Cm)** | 0.254 | 0.061 | 1.776 | 0.595 | 3.011 |
| **High FiO2 baseline** | 0.120 | 0.505 | 2.887 | 0.623 | 4.262 |
| **High FiO2 before extubation** | 0.201 | 0.289 | 2.818 | 0.563 | 4.187 |
| **High MAP baseline** | 0.634 | 0.071 | 0.924 | 0.542 | 1.576 |
| **High MAP before extubation** | **0.510** | **0.016*** | **3.859** | **2.050** | **7.262** |
| **SIMV Mode** | **1.350** | **0.001*** | **5.237** | **2.089** | **10.367** |
| **Low PO2 baseline** | **1.817** | **<0.001**** | **6.151** | **2.165** | **17.477** |
| **Low PO2 before extubation** | 0.127 | 0.345 | 1.704 | .783 | 3.707 |

AOR: adjusted odds ratio, CI: Confidence interval.

The best cutoff of baseline oxygenation index in prediction of failed extubation is ≥23.95 with AUC 0.852, 85.7% sensitivity, 84.2% specificity, 85.7% PPV, 84.2% NPV and overall accuracy 85% (P<0.001). The best cutoff of oxygenation index 1 hour before extubation in prediction of failed extubation is ≥4.75 with AUC 0.852, 85.7% sensitivity, 84.2% specificity, 85.7% PPV, 84.2% NPV and overall accuracy 85% (P<0.001).

The best cutoff of baseline RSS in prediction of failed extubation is ≥8.19 with AUC 0.888, 81% sensitivity, 78.9% specificity, 81% PPV, 78l.9% NPV and overall accuracy 82.5% (P<0.001). The best cutoff of RSS 1 hour before extubation in prediction of failed extubation is ≥2.63 with AUC 0.782, 81% sensitivity, 73.7% specificity, 77.3% PPV, 77.8% NPV and overall accuracy 77.5% (P=0.002). The best cutoff of baseline RSS/kg in prediction of failed extubation is ≥3.38 with AUC 0.97, 95.2% sensitivity, 89.5% specificity, 90.9% PPV, 94.4% NPV and overall accuracy 92.5% (P<0.001).

The best cutoff of RSS/kg 1 hour before extubation in prediction of failed extubation is ≥1.35 with AUC 0.952, 90.5% sensitivity, 94.7% specificity, 95% PPV, 90% NPV and overall accuracy 92.5% (P<0.001). The best cutoff of baseline $PO_2$ in prediction of failed extubation is ≤44.1with AUC 0.81, 81% sensitivity, 68.4% specificity, 73.9% PPV, 76.5% NPV and overall accuracy 75% (P<0.001) (**Table 8**).

**Table (8):** Performance of different parameters baseline and 1 hour before extubation in prediction of failed extubation.

| **Variable** | **Cutoff** | **AUC** | **Sensitivity** | **Specificity** | **PPV** | **NPV** | **Accuracy** | P-value |
|---|---|---|---|---|---|---|---|---|
| Oxygenation index **Baseline** | ≥23.95 | 0.858 | 85.7% | 84.2% | 85.7% | 84.2% | 85% | <0.001** |
| Oxygenation index **Before extubation** | ≥4.75 | 0.852 | 85.7% | 84.2% | 85.7% | 84.2% | 85% | <0.001** |
| RSS baseline at **Baseline** | ≥8.19 | 0.888 | 81% | 78.9% | 81% | 78.9% | 82.5% | <0.001** |
| RSS baseline **Before extubation** | ≥2.63 | 0.782 | 81% | 73.7% | 77.3% | 77.8% | 77.5% | 0.002* |
| RSS/kg at **Baseline** | ≥3.38 | 0.97 | 95.2% | 89.5% | 90.9% | 94.4% | 92.5% | <0.001** |
| RSS/kg **Before extubation** | ≥1.35 | 0.952 | 90.5% | 94.7% | 95% | 90% | 92.5% | <0.001** |
| PO2 at **Baseline** | ≤44.1 | 0.81 | 81% | 68.4% | 73.9% | 76.5% | 75% | <0.001** |

AUC: Area under curve. PPV: Positive predictive value. PPV: Positive predictive value. **P≤0.001 is statistically highly significant.

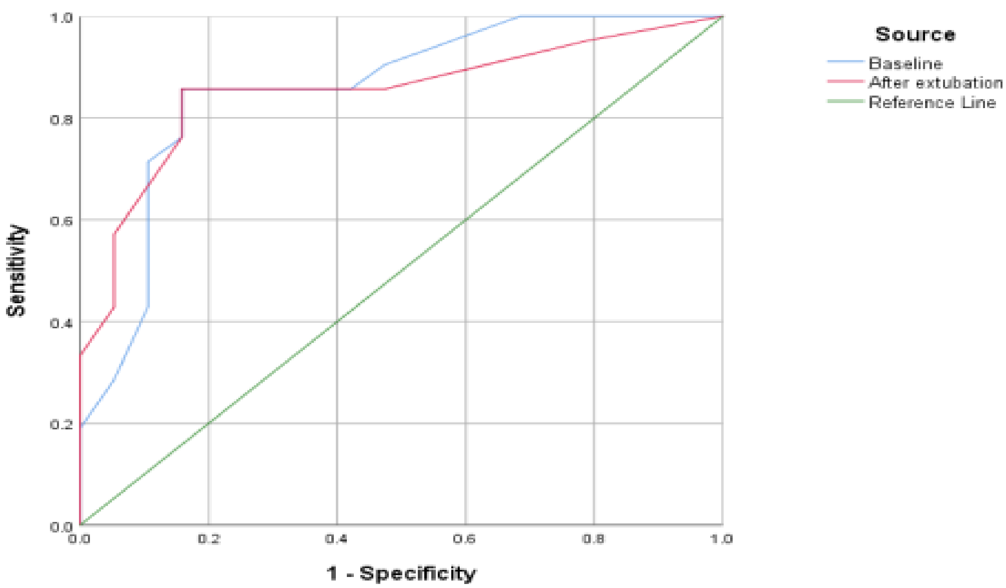


**Figure (1):** ROC curve showing performance of Oxygenation index baseline and 1 hour before extubation in prediction of failed extubation.

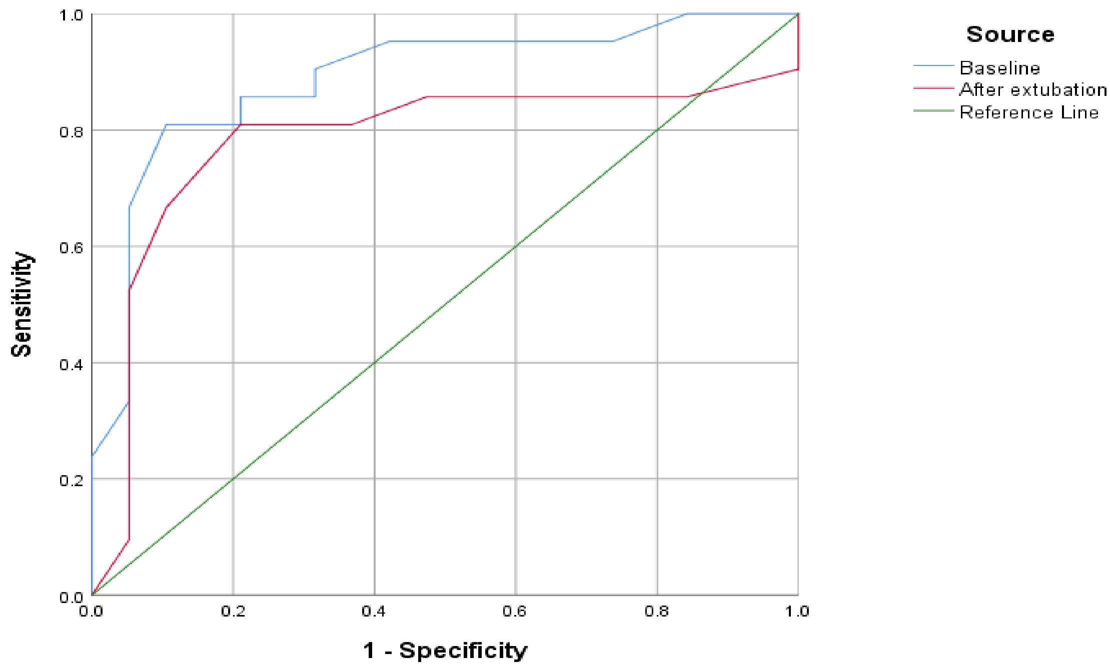


**Figure (2):** ROC curve showing performance of RSS baseline and 1 hour before extubation in prediction of failed extubation.

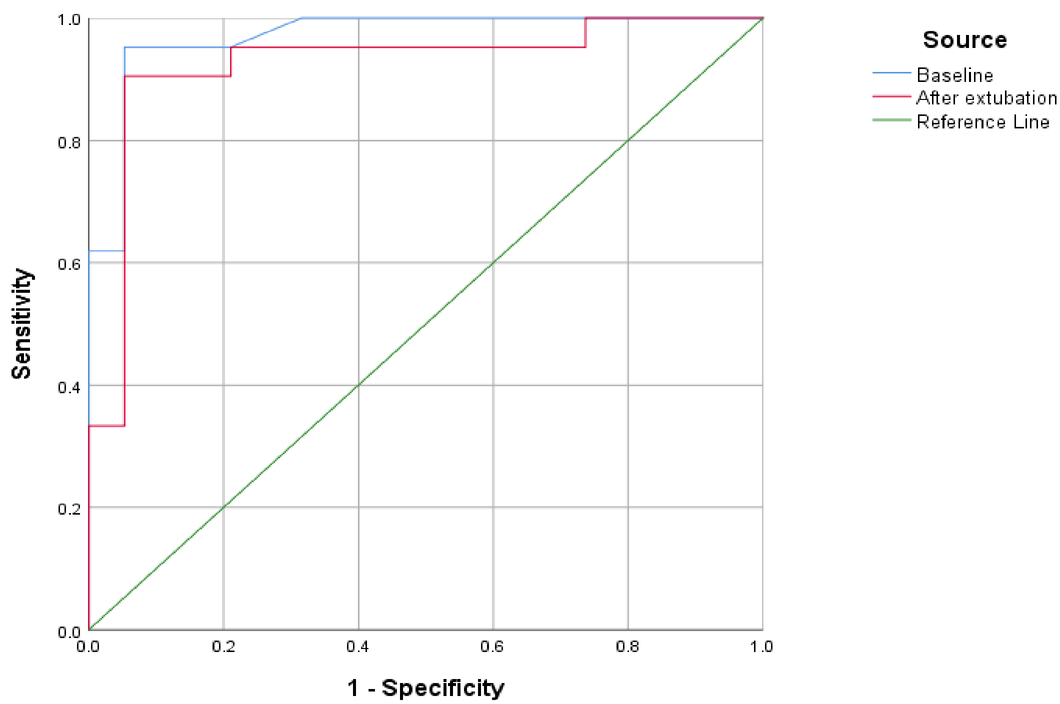


**Figure (3):** ROC curve showing performance of RSS/kg baseline and 1 hour before extubation in prediction of failed extubation.

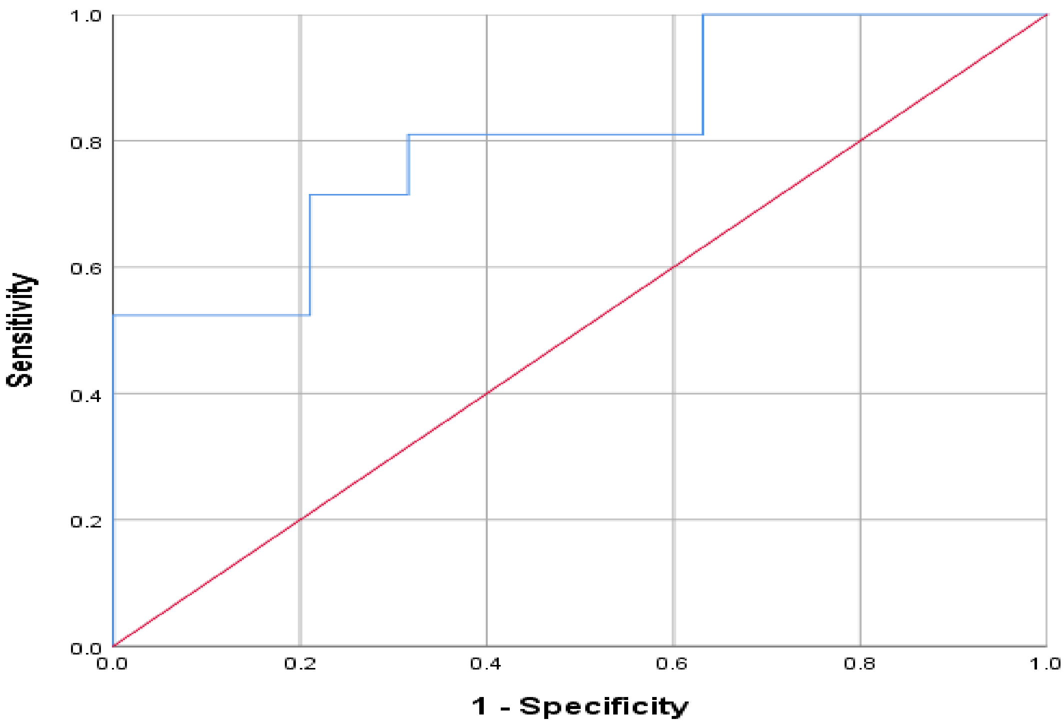


**Figure (4):** ROC curve showing performance of PO2 baseline in prediction of failed extubation.

On doing univariate analysis of studied parameters, it was found that baseline OI≥3.95, OI 1 hour before extubation ≥4.75 significantly increased risk of failed extubation by 32 and 32 folds respectively. Baseline RSS≥819, RSS 1 hour before extubation ≥262.5 significantly increase risk of failed extubation by 15.937 and 11.9 folds respectively. RSS/kg baseline ≥ 3.38, on using univariate analysis, significantly increase risk of failed extubation by 170 folds while on applying multivariate backward regression analysis, it significantly increases risk by 35.52 folds. RSS/kg 1 hour before extubation ≥1.53 ,on using univariate analysis, significantly increase risk of failed extubation by 171 folds while on applying multivariate backward regression analysis, it significantly increases risk by 34.4 folds (**Table 9**).

**Table (9):** Univariate and multivariate analysis of oxygenation index, RSS and RSS/kg in prediction of failed extubation.

| Variable | COR | 95% CI | P-value |
|---|---|---|---|
| **Oxygenation index baseline ≥23.95** | 32 | 5.64 – 181.63 | <0.001** |
| **OI 1 hour before extubation ≥4.75** | 32 | 5.64 – 181.63 | <0.001** |
| **RSS baseline≥819** | 15.937 | 3.38 – 75.1 | <0.001** |
| **RSS before ≥262.5** | 11.9 | 2.67 – 52.96 | 0.001** |
| **RSS/kg baseline≥3.38** | 170 | 14.51 – 2042.24 | <0.001** |
| **RSS/kg before ≥1.35** | 171 | 14.24 – 2053.25 | <0.001** |
| **Multivariate backward regression analysis** | | | |
| **Variable** | **AOR** | **95% CI** | **P-value** |
| **RSS/kg baseline≥3.38** | 35.52 | 1.99 – 633.14 | 0.015* |
| **RSS/kg before ≥1.35** | 34.4 | 1.89 – 625.03 | 0.017* |

COR Crude odds ratio. **P≤0.001 Statistically highly significant. AOR Adjusted odds ratio. CI confidence interval.

**DISCUSSION**

Concerning the outcome, the present study showed that on trial of extubation, 52.5% failed extubation and need reintubation, while 47.5% succeeded.

In agreement with our results, existing research indicates a significant prevalence of EF in premature newborns. **Chawla *et al.*** **[7]** (28 weeks GA) found that the EF rate within 5 days was 37-50 % in premature newborns.

In addition, according to **Stefanescu *et al.*** **[16]**, 40% was the EF rate in preterm infants was. Also, **Shalish *et al.*** **[17]** (≤1,250 grams BW) demonstrated that the cumulative EF rate was high through 3-7 days following extubation.

Concerning cause of respiratory failure in our study, 14.3%, 14.3%, 14.3%, 9.5%, 9.5%, 9.5%, 9.5% and 9.5% had failure due to apnea, hemodynamic instability, hypoxemia, clinical instability, combined hypoxemia and sepsis, sepsis, undefined, recurrent intubation and pneumothorax respectively.

In line with the current findings, the most prevalent reintubation causes according to **Mandhari *et al.*** **[18]**, were bradycardia and desaturation (50%), apnea (17.7%) & respiratory failure (11.8%).

In accordance with the current findings, as demonstrated by **Cheng *et al.*** **[19]**, 65.71% experienced $CO_2$ retention or/and hypoxemia involving severe infection (31.43%), 34.29% had considerable apnea and bradycardia, atelectasis (20%), and pulmonary bleeding (14.29%).

There was a **significant** relation between extubation outcome and GA and pre-intubation support duration (were significantly lower in those with unsuccessful extubation). The relation between outcome age at intubation and respiratory support was **insignificantly** different. Similarly, the relationship between BW and EF is consistent with previously published research indicating that a lower BW is associated with a higher risk of EF **[17,20,21]**.

**Mandhari *et al.*** **[18]** showed that the ES group had higher GA than the EF group, which is consistent with the current findings. This was significantly different between the EF and ES groups, whereas BW, intubation weight, and extubation weight were comparable between both groups. The lack of association between the median BW and EF is due to the fact that the BWs were consistently greater (>1,000 g).

Our results demonstrated a **significant** relation between outcome and antenatal steroids utilization (significantly related with extubation success). There was an **insignificant** relation between outcome and maternal risk factors.

In disagreement with our study, **Wang *et al.*** **[21]** reported that antenatal steroids utilization was insignificantly different between ES and EF.

Our findings revealed a **significant** relationship between outcome and cardiological lesions and the Down score (higher scores associated with failure) and an **insignificant** relationship between outcome and the occurrence of sepsis, intractable apnea, or pulmonary hypertension.

**Mandhari *et al.*** **[18]** revealed that cardiological lesions, including PDA were significantly different between EF and ES groups. These findings are consistent with the current findings. EF group showed a considerably higher PDA prevalence than in the ES group (78.9% vs. 40%, P=0.03).

**Ishak *et al.*** **[22]** reported that an insignificant difference between outcome (ES and EF) and diagnosis (pneumonia, disturbed conscious level, aspiration, acute renal failure, Guillain Barre Syndrome, and diabetic ketoacidosis) among patients.

Concerning relation between outcome of extubation and ventilation-related parameter, there was statistically **significant** relation between outcome and duration of pre-intubation support (significantly lower in patients with failure), size and length of tube (significantly lower in patients with failure). There was statistically **non-significant** relation between outcome and either need for respiratory support, age at intubation or receiving Surfactant. There was statistically **significant** relation between outcome and all of mode of MV, FiO2, and mean airway pressure baseline and 1 hour before extubation (FiO2 and MAP were **significantly** higher among patients with failed extubation both baseline and 1 hour before extubation). There was statistically **non-significant** relation between outcome and all of type of MV, duration of first intubation, and PEEP, PIP baseline and 1 hour before extubation. Within each group, there was significant decrease in PIP, PEEP, FiO2, and MAP 1 hour before extubation as compared to baseline values.

**Mandhari *et al.*** **[18]** found that infants with EF had significantly elevated total MV days and a longer hospital stay than those with ES. Other clinical variables (age & weight at intubation and extubation, caffeine use, pre-extubation hemoglobin level) as well as intraventricular hemorrhage rate, pre-extubation ventilatory variables (mode, Vt, PIP, PEEP, RR, FiO2), and pre-extubation blood gas results were insignificantly different.

In accordance with the present results, **Soliman *et al.*** **[23]** found significant differences between the outcomes (ES and EF) and MAP, MV & oxygen support duration.

Respecting the relation between outcome of extubation and ABG baseline and 1 hour before extubation, there was **significant** relation between outcome and PO2 baseline and 1 hour before extubation (FiO2 and MAP were **significantly** lower among patients with failed extubation both baseline and 1 hour before extubation). There was statistically **insignificant** relation between outcome and either HCO3, $PaCO_2$ or PH baseline and 1 hour before extubation. Within each group, there is significant decrease in PH, PaCO2, and PO2, 1 hour before extubation as compared to baseline values. Within patients with failed outcome, there is significant increase in HCO3 1 hour before extubation while among groups with succeed extubation, there is non-significant increase in HCO3.

In agreement with the current findings, **Mhanna *et al.*** [9] showed that FiO2 and PIP were significantly different between ES and EF groups at the moment of extubation. Also, A shorter time of stay on MV was associated with greater extubation success. pH and $CO_2$ levels prior to extubation were not substantially linked with EF, according to **Wang *et al.*** [21].

Regarding pH, our results disagreed with **Gupta *et al.*** [23] who reported that pH was significantly different between EF and ER groups. Respecting PaCo2, our results agreed with **Gupta *et al.*** [23] showing that PaCo2 was insignificantly different between both groups.

Regarding the relation between outcome of extubation and RSS, RSS/kg baseline (at intubation) and 1 hour before extubation, there was statistically **significant** relation between outcome and RSS and RSS/kg baseline and 1 hour before extubation (RSS and RSS/kg baseline and 1 hour before extubation were **significantly** higher among patients with failed extubation both baseline and 1 hour before extubation). Within each group, there is significant decrease in RSS and RSS/kg 1 hour before extubation as compared to baseline values.

In accordance with the present results, **Gupta *et al.*** [23] reported that RSS in first 6 hours and pre-extubation RSS was significantly different between EF and ER groups. Respiratory rate before extubation was comparable between EF and ER groups as demonstrated by **Wang *et al.*** [21]**.**

Respecting the relation between outcome of extubation and oxygenation index baseline and before extubation, there was statistically **significant** relation between outcome and oxygenation index baseline and 1 hour before extubation (oxygenation index was **significantly** higher among patients with failed extubation both baseline and 1 hour before extubation). Within each group, there was significant decrease in oxygenation index 1 hour before extubation as compared to baseline values.

Previous research has linked higher GA, higher postmenstrual age, lower PaCO2, lower FiO2, lower oxygenation index with successful extubation [7,20,24]**.**

The present study showed that, Non-use of antenatal steroid, higher down score, and higher MAP before extubation, SIMV mode and low baselinePO2 increase risk of failure by 3.70, 6.28, 3.86, 5.24 and 6.15 folds, respectively.

Our results were not compatible with the study by **Manley *et al.*** [24] on extremely preterm newborns (<28 weeks GA) revealed that a greater GA was related with ES. This was likely attributable to the research population's composition. In obstetrics, abortion is the termination of a pregnancy with a fetal GA <28 weeks. Frequently, fetuses with a younger GA or diminished viability after delivery are more likely to be terminated or abandoned by their parents. Consequently, the younger the fetal GA, the less likely it was to be sent to the NICU and undergo MVEI.

According to **Dimitriou *et al.*** [25], GA< 30 weeks) and postnatal age were more important risk factors than respiratory muscle strength and respiratory load measures. **Szymankiewicz *et al.*** [26] evaluated the pulmonary mechanics of VLBW babies before extubation and found that patients with SE had considerably improved pulmonary function values and comparable clinical features compared to patients with unsuccessful extubation. In the study by **Hermeto *et al.*** [20], such precautions were not routinely implemented prior to extubation. Based on the collected data, we determined that the percentage of extubation failure was affected by GA, BW & 5-minute Apgar score. However, after doing the logistic regression analysis, only GA was found to be statistically significant between the analyzed groups.

**Mandhari *et al.*** [18] observed that only GA <28 weeks remained as a significant predictor of EF following multivariate analysis; the 1-minute Apgar score and PDA were no longer linked with EF.

The best cutoff of baseline oxygenation index in prediction of failed extubation is ≥23.95 with AUC 0.852, 85.7% sensitivity, 84.2% specificity, 85.7% PPV, 84.2% NPV and overall accuracy 85% (P<0.001). The best cutoff of oxygenation index 1 hour before extubation in prediction of failed extubation is ≥4.75 with AUC 0.852, 85.7% sensitivity, 84.2% specificity, 85.7% PPV, 84.2% NPV and overall accuracy 85% (P<0.001).

The best cutoff of baseline RSS/kg in prediction of failed extubation showed 95.2% sensitivity, 89.5% specificity, 90.9% PPV, 94.4% NPV and overall accuracy 92.5% (P<0.001). The best cutoff of RSS/kg 1 hour before extubation in prediction of failed extubation is ≥135.38 with AUC 0.952, 90.5% sensitivity, 94.7% specificity, 95% PPV, 90% NPV and overall accuracy 92.5% (P<0.001). On doing univariate analysis of studied parameters, it was found that baseline OI≥3.95, OI 1 hour before extubation ≥4.75 significantly increased risk of failed extubation by 32 and 32 folds respectively. Baseline RSS≥819, RSS 1 hour before extubation ≥262.5 significantly increase risk of failed extubation by 15.937 and 11.9 folds respectively. RSS/kg baseline ≥ 337.91, on using univariate analysis, significantly increase risk of failed extubation by 170 folds while on applying multivariate backward regression analysis, it significantly increases risk by 35.52 folds. RSS/kg 1 hour before extubation ≥34.4,on using univariate analysis, significantly increase risk of failed extubation by 171 folds while on applying multivariate backward regression analysis, it significantly increases risk by 34.4 folds.

The best cutoff of baseline PO2 in prediction of failed extubation is ≤44.1with AUC 0.81, 81% sensitivity, 68.4% specificity, 73.9% PPV, 76.5% NPV and overall accuracy 75% (P<0.001).

## CONCLUSION

In preterm infants, $O_2$ saturation, Pa $Co_2$, tidal volume, and RSS had high sensitivity and specificity in predicting extubation failure.

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