Early Human Development 166 (2022) 105552

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Regional pulmonary oxygen saturations immediately after birth

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ARTICLE INFO

Keywords:
Neonate
Near-infrared spectroscopy
Lung

ABSTRACT

Background: Partial oxygen saturation (SpO_2) increases within minutes during transition from the intrauterine to extrauterine life. This study aims to determine the postnatal course of pulmonary regional oxygen saturation (rSO_2) measured by Near-Infrared Spectroscopy (NIRS).
Methods: We conducted an observational study at the delivery room in infants above 35 weeks of gestation who did not need resuscitation and did not develop respiratory distress. Preductal pulse oximetry (Covidien Nellcor™) and right pulmonary apex oxygen saturation ($raSO_2$) and basal oxygen saturation ($rbSO_2$) (Covidien INVOS™) were measured, starting from the postnatal third minute of life, until the 15th minute. The correlations between SpO_2 and pulmonary rSO_2 were analyzed.
Results: Of the 110 infants included in the study, 87 were term and 23 were late preterms. The gestational age and birth weight were 38.5 ± 1.36 weeks and 3285 ± 508 g, respectively. Median (5th–95th percentile) $raSO_2$ and $rbSO_2$ were 79% (58–95%) and 78% (46–95%) at the third minute, respectively. The rSO_2 values measured from both sides increased and reached a steady-state around postnatal 9 min, similar to SpO_2 values. The pulmonary NIRS values were significantly higher for babies born by C-Section compared to babies born by vaginal delivery ($p < 0.05$).
Conclusion: We found that rSO_2 measurements increased within minutes in the postnatal period in late preterm and term babies without respiratory distress and reached a plateau at the postnatal 9th minute. The normal values obtained from this preliminary study may be used to predict the prognosis of cases with respiratory distress.

1. Introduction

The transition from intrauterine to extrauterine life depends on complex physiological changes in the cardiovascular and respiratory systems [1]. Newborn oxygen saturations increase progressively within a few minutes with the progressive aeration of the lungs [2]. After birth, preductal oxygen saturations are typically 60–70% at 1–2 min, rising to 80–90% at 5 min [2]. The median time required to reach 90% SpO_2 was 7.9 min in the study reported by Dawson [3].

Near-infrared spectroscopy (NIRS) is an easily applicable, non-invasive, painless continuous monitoring tool which is widely used in neonatal intensive care units and accepted as a standard of care for monitoring blood oxygen saturation mainly in the brain, kidney, and mesentery. Regional oxygen saturation (rSO_2) directly reflects the oxygenation and oxygen metabolism of the tissue [4]. Cerebral and mesenteric NIRS has been increasingly and more widely used in critically ill neonates for monitoring the balance between tissue oxygen delivery and consumption, providing cerebral and somatic oximetry values, and allowing earlier identification of abnormalities in hemodynamics and cerebral perfusion [5]. However, there is very limited data about the clinical application of pulmonary NIRS in neonates, especially during the transition period.

The primary aim of this prospective study was to define the reference ranges for regional lung tissue oxygen saturation measured from two sites: the apex and basal pulmonary regions, during the immediate neonatal transition period in term and late preterm newborns who did not need any cardio-respiratory support and/or resuscitation. The aim of this study was to create reference ranges and centile charts of regional pulmonary oxygenation during the first 15 min immediately after birth and evaluate the correlation between pulmonary NIRS and SpO_2

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https://doi.org/10.1016/j.earlhumdev.2022.105552
Received 28 September 2021; Received in revised form 31 January 2022; Accepted 1 February 2022
Available online 5 February 2022

measurements. To the best of our knowledge, this is the first study that evaluates regional lung oxygenation during the neonatal transition period in healthy newborns.

2. Methods

This prospective observational study was conducted between January and October 2020 at the two training and research hospitals. The study protocol and the parental consent form were approved by the local ethics committee. The study was conducted following the principles of the Declaration of Helsinki.

We included infants >35 weeks of gestation who fulfilled the inclusion criteria and written informed consent was obtained from the parents before birth. Resuscitation protocols were performed following the NRP guidelines. Infants who need respiratory support and/or resuscitation in the delivery room, infants with congenital malformations, or chromosomal/syndromal abnormalities were excluded. Antepartum medical history, perinatal data, including gestational age, birth weight, gender, mode od delivery, umbilical artery pH, base excess, cord blood hemoglobin values, APGAR scores were all recorded. All babies were observed for 15 min, starting from the 3rd minute after birth. Measurements were obtained simultaneously by a pulse oximeter (heart rate and preductal arterial oxygen saturation (SpO_2) from the right wrist (Nellcor) and a NIRS monitor (INVOS 5100c monitor, Medtronic, Minneapolis, MN, USA) starting from the postnatal 3rd min up to the 15th min and the values were recorded every minute. Peripheral oxygen saturation and heart rate were measured continuously with pulse oximetry and the data was transferred to the computer. The neonatal NIRS sensor was positioned on the right lung apex ($raSO_2$) (second intercostal space) and basal lung area ($rbSO_2$) (seventh intercostal space).

Statistical analysis was performed with the STATA version 15.1 (Stata Corp, College Station, Tex). We analyzed the data, according to gender and delivery modes (normal spontaneous vaginal delivery (NSVD) and Cesarean section (C/S)). The normality assumption for continuous variables was tested with Kolmogorov Smirnov, skewness and kurtosis tests, and also with histogram plots. We compared the measurements obtained from the apex and basal, for gender and mode of delivery, using the Mann Whitney *U* test. For the development of linear models, the data were transformed into longitudinal data, where two models were developed for the prediction of saturation variable by using either apex or basal measurement as the independent variable. These models were created for both strata of genders and delivery types, separately. A *p*-value less than 0.05 was considered statistically significant.

3. Results

During the study period, 128 measurements were performed and 18 infants were excluded due to respiratory distress. Of the 110 infants included in the study, 87 were term and 23 were late preterm babies. The gestational age and birth weight were 38.5 ± 1.36 weeks and 3285 ± 508 g, respectively. Of these infants, 60% were delivered by C/S and 54.5% were male. APGAR scores at 1 min and 5 min were 9 (5–9) and 10 (8–10), respectively. Cord blood gas of 24 babies could not be obtained. Mean umbilical artery pH and base excess of the infants were 7.35 ± 0.06 and − 1 ± 2.95 mmol/L, respectively. The mean cord hemoglobin value was 16.7 ± 1.63 g/dL (Table 1).

Heart rate was always above 100 beats per minute in the whole study group. Preductal SpO_2 could not be measured in 7 and 4 cases at the 3rd and 4th minutes, respectively. At 3 min, the preductal median (5th–95th percentiles) SpO_2 was 80% (66–92%), reached 85% (73–94%) by 4 min, 90% (82–96) by 5 min and continued to rise to a median of 98% (91–100%) at 15 min (Fig. 1). SpO_2 levels reached a steady-state around 9 min. The 4th, 5th, and 6th minute SpO_2 levels were significantly higher in those babies born by NSVD compared to those born by C/S ($p < 0.05$). When the measurements were compared according to gender, boys had significantly higher SpO_2 values at 8, 10 and 15 min compared to girls, but no such difference was detected at other times (Fig. 2).

Table 1
Demographic data of the study group.

Sex (Male) (%)	60 (54.5)
Mode of delivery (C/S) (%)	66 (60)
Gestational age (week)	38.5 ± 1.36
Birth weight (g)	3285 ± 508
Birth length (cm)	50.7 ± 1.9
Head circumference (cm)	34.6 ± 0.95
APGAR 1 min	9 (5–9)
APGAR 5 min	10 (8–10)
pH	7.35 ± 0.06
Base excess (mmol/L)	−1 ± 2.95
Cord hemoglobin value (g/dL)	16.7 ± 1.63
Maternal disease (n) (%)	14 (12.7)
Hypothyroidism	5
Diabetes mellitus	3
Behcet's disease	2
Epilepsy	2
Asthma	2

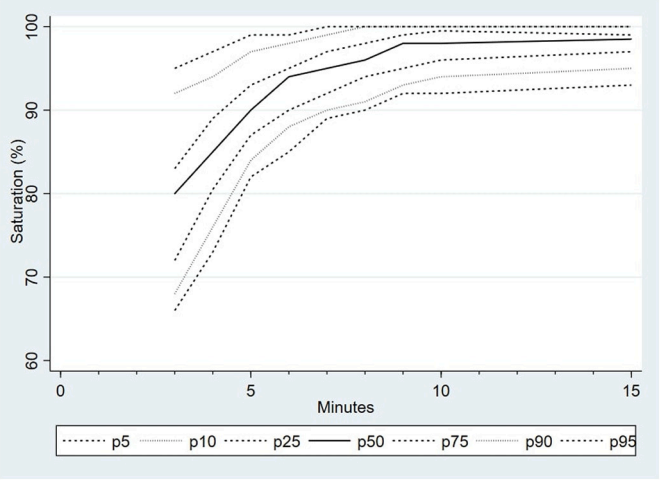

Fig. 1. Graph of changes in saturation in minutes and the percentiles of babies.

Regional NIRS could not be measured in 9 and 6 cases at the 3rd and 4th minutes, respectively. Apex measurements were always higher than the basal area during all measurements. The $raSO_2$ and $rbSO_2$ were 79% (58–95%) and 78% (46–95%) at 3 min respectively, increased to 83% (63–95%) and 79% (47–95%) at 4 min, 85% (66–95%) and 84% (55–95%) at 5 min. The postnatal increase reached a steady-state around 9 min (Fig. 3).

We developed 10 distinct models for the prediction of saturation values in distinct population groups. Due to the correlation between the apex and basal measurements ($r = 0.655$, $p < 0.001$), only one predictor was allowed to use in these linear models. For the whole study population, apex measurement had a coefficient of 0.409 (95% CI 0.361–0.457) and the model had a r2 value of 0.170 (Table 2). While there was no significant difference in the comparison of measurements according to gender (Fig. 4), a significant difference was found according to the mode of delivery. The $raSO_2$ and $rbSO_2$ measurements of the babies who were born via C/S were significantly higher at minutes 5,6,7,8,9,10, and 15 ($p < 0.05$) (Fig. 5).

4. Discussion

Regional saturation monitors, also known as NIRS monitors, are currently available within delivery rooms and NICUs to monitor regional saturations across time [6]. NIRS technology is a very well suited tool for newborns. So far, the brain remains the most extensively

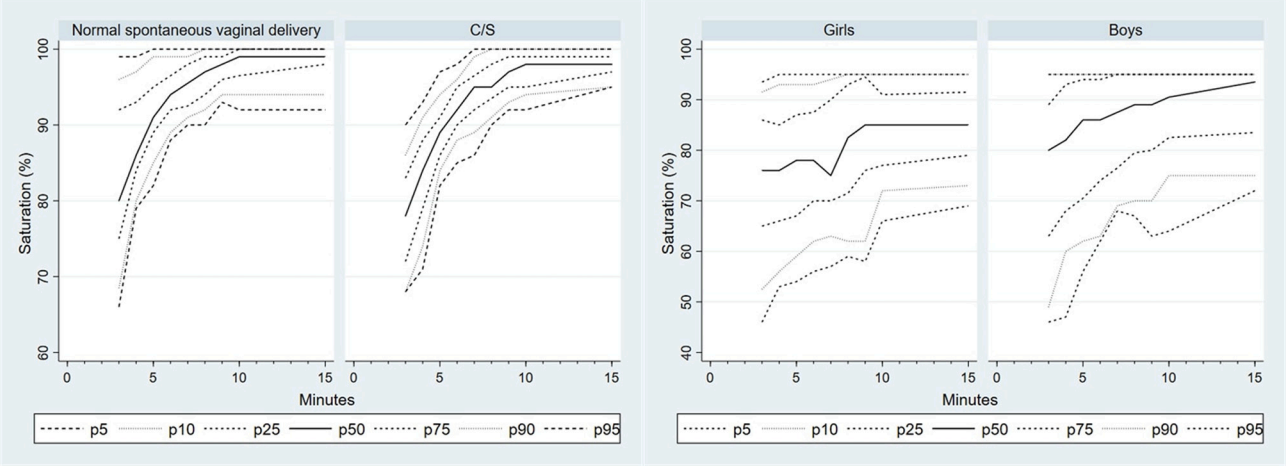

Fig. 2. Saturations according to the mode of delivery and gender.

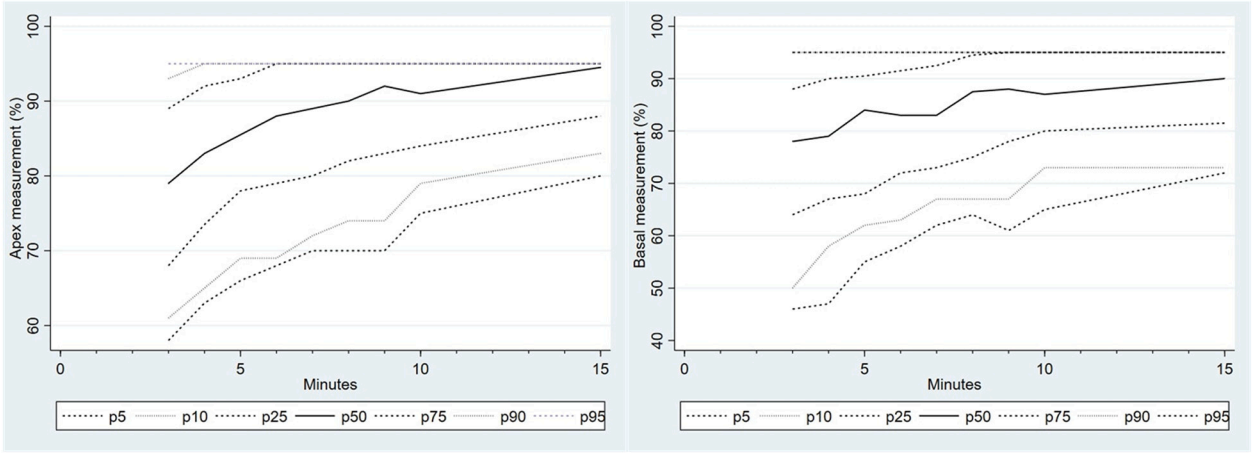

Fig. 3. The percentiles of right pulmonary apex and basal regional oxygen saturations (raSO2 and rbSO2).

Table 2
Linear models for the prediction of saturation.

Population	Independent variable	Coefficient	Confidence Interval (95%)		*P* value	r^2
Study population	Apex	0.409	0.361	0.457	<0.001	0.170
Study population	Basal	0.297	0.257	0.337	<0.001	0.146
Female	Apex	0.413	0.349	0.476	<0.001	0.211
Male	Apex	0.395	0.324	0.467	<0.001	0.138
Female	Basal	0.286	0.236	0.337	<0.001	0.191
Male	Basal	0.297	0.235	0.359	<0.001	0.105
NSVD	Apex	0.284	0.211	0.357	<0.001	0.099
C/S	Apex	0.516	0.456	0.577	<0.001	0.296
NSVD	Basal	0.264	0.205	0.323	<0.001	0.125
C/S	Basal	0.323	0.273	0.374	<0.001	0.199

studied organ by NIRS in newborns, followed by mesenteric, renal, and skeletal muscle beds [7,8]. Several studies have been conducted to show the changes of oxygenation during the transition period in those regions [9–12]. The establishment of those percentiles in healthy newborns aimed to predict the forthcoming pathologies and prognosis of certain diseases, and are also used for the decision of intervention during the immediate postnatal adaptation period [12–14]. Pichler et al. [13] established reference ranges to help prevent cerebral hypo- and hyperoxygenation during the transition period. In the study in which 100 healthy preterm and term babies were followed up for the first 6 h, cranial NIRS percentiles were created [13]. Apart from cranial measurements, NIRS is also being investigated in the somatic and renal areas. It is thought that somatic measurements may be more realistic in newborns, as opposed to adults, due to fewer fat layers and muscles [15]. It has recently been reported that pulmonary NIRS might reflect the actual oxygenation of lung tissue in premature infants [4]. However, there is no study that evaluated the reference pulmonary NIRS values in neonates during the transition period. Therefore, we performed this prospective study and established the pulmonary oxygenation percentilles in term and late preterm infants.

In an observational study of 61 infants from birth to the first 9 h of life, the mean cranial rSO_2 increased rapidly from 2 min to 7 min without any other change in term babies delivered by elective C/S, while the mean renal rSO_2 and mean splanchnic rSO_2 increased for 10 min and

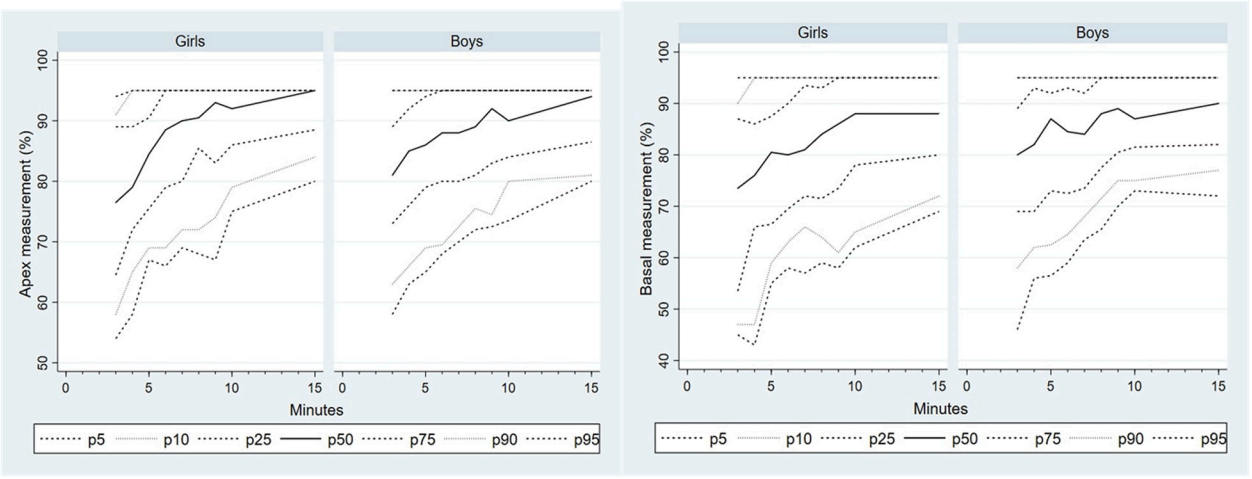

Fig. 4. Regional apex and basal oxygen saturation measurements for gender.

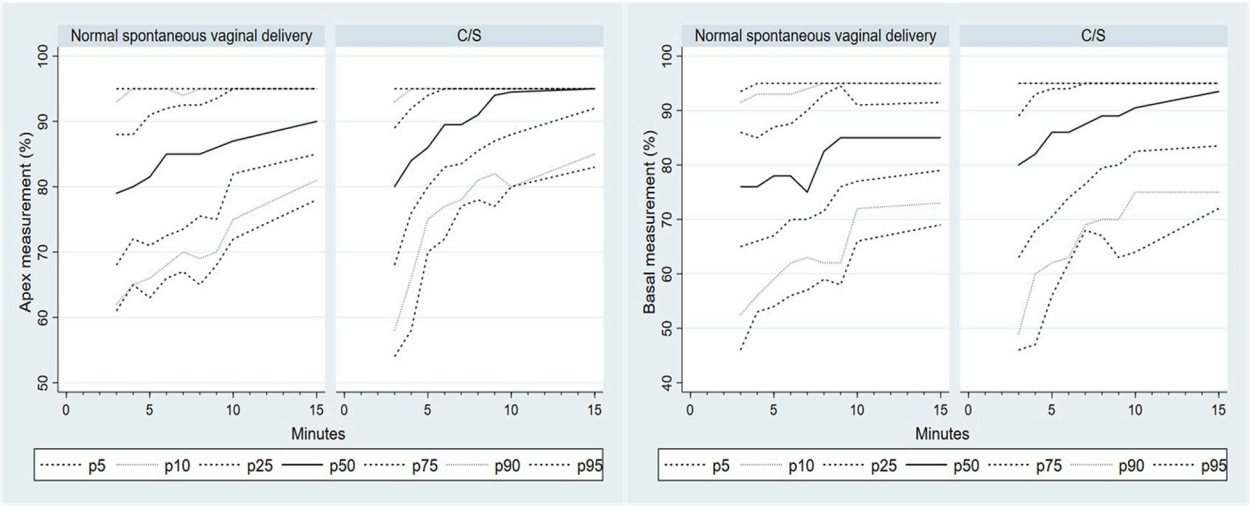

Fig. 5. Regional apex and basal oxygen saturation measurements according to the mode of delivery.

then remained stable [11]. Similarly, pulmonary NIRS measurements increased within minutes in the postnatal period in late preterm and term babies without respiratory distress and reached a plateau at the postnatal 9th minute in our study.

The aim of our study was to evaluate pulmonary rSO_2 values during the transition period in late preterm and term babies and compare it with SpO_2 measurements. For a successful transition from the fetal period to the neonatal period, lung fluid should be cleared and functional residual capacity should be established. In Dawson's study, a median of 7.9 min (IQR 5–10 min) was required to reach a SpO_2 value of >90% [3]. Other studies reported similar results changing between 8 and 15 min [16–20]. In our study, we found that the oxygen saturation reached 90% at the 5th minute and 95% at the 7th minute, similar to the studies reported from the literature [16–20].

In our study, we found that SpO_2 was significantly higher in those born by NSVD compared to those born by C/S at the 4th, 5th, and 6th minutes. Several studies also reported similar results [10,16,20]. Contrary to these studies, there are also studies that could not find any difference between the two delivery modes [21,22]. Therefore, more clinical studies including larger number of infants are required to establish the effect of mode of delivery on SpO_2 levels during the transition period.

Our study aimed to define reference ranges and centile charts for the regional lung tissue measured from two sites (the apex and basal lung region). In a study conducted by Yang et al. [4] evaluating the actual pulmonary oxygenation status of the premature babies, a positive linear correlation was found between pulmonary rSO_2 and SpO_2 levels in preterm babies who did not receive oxygen therapy. In our study, $raSO_2$ and $rbSO_2$ were measured in infants without respiratory support and reached a plateau at the same time as SpO_2 in approximately 9 min. SpO_2 values of late preterm and term babies were found to be correlated with apex and basal NIRS measurements. Therefore, we suggest that NIRS may clinically be used for monitorization of pulmonary tissue oxygenation in neonates. We also established reference pulmonary oxygenation percentilles during the transition period in term and late preterm infants. However, clinical studies including larger number of infants with and without respiratory distress with a longer follow-up time are required to establish the role of pulmonary NIRS values for clinical use in neonates.

Delayed maturation of lung structure and function causes inhibition of postnatal adaptation and causes problems such as respiratory distress to be seen more frequently in boys [23]. However, we did not find any significant difference between the lung measurements and gender.

Both $raSO_2$ and $rbSO_2$ measurements after the 4th minute of life were significantly higher in babies born by C/S in our study. As there are no other studies evaluating pulmonary rSO_2 levels, we are not able to

compare our data with previous studies. However, as pulmonary NIRS values correlated well with SpO_2 values in this study, our results were in agreement with studies that reported higher SpO_2 values in infants born by C/S [24,25]. In contrast, some studies reported higher SpO_2 values in infants born by NSVD [20,26]. Therefore, recent clinical studies including larger number of infants are required to identify the role of mode of delivery on both cerebral and pulmonary oxygenation during the transition period.

The small sample size and the inability to perform other regional measurements simultaneously can be stated as the limitations of our study. Searching through the literature, we could find only one study on regional pulmonary NIRS in newborns [4]. Therefore, we were unable to discuss the available data with the literature.

As far as we know this is the first study on regional pulmonary SO_2 in late preterm and term neonates without respiratory distress during the transitional period, just after birth. The impact of pulmonary NIRS monitoring and interventions on short- and long-term outcomes in neonates during the transition and postnatal period still need to be studied. Our next step will be a larger randomized controlled trial for the evaluation of those centiles in babies with respiratory distress, for the decision of early intervention and for the prediction of their outcomes as well.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Sinem Gulcan Kersin: Writing- Reviewing and Editing, data curation. Beril Yaşa: Data curation. Merih Çetinkaya: Investigation, project administration, methodology. Can Ilgın: Formal analysis, software. Eren Özek: Conceptualization, supervision. Hülya Bilgen: Investigation, project administration, supervision.

Declaration of competing interest

None to declare.

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