ORIGINAL ARTICLES

Delayed vs Immediate Cord Clamping Changes Oxygen Saturation and Heart Rate Patterns in the First Minutes after Birth

Celia Padilla-Sánchez, CNM[1,2,3], Susana Baixauli-Alacreu, CNM[1,2,3], Antonio José Cañada-Martínez, MSN[4], Álvaro Solaz-García, MSN[5], Maria José Alemany-Anchel, PhD[6], and Máximo Vento, MD, PhD[1,6]

Objective To build arterial oxygen saturation (SpO_2) and heart rate (HR) percentiles for the first 10 minutes after birth in term infants born after an uneventful gestation, vaginal delivery, and delayed cord clamping (DCC) for ≥60 seconds, and to compare our results with previous ones constructed after immediate cord clamping.

Study design Preductal SpO_2, HR, and timing of DCC immediately after complete fetal body expulsion were recorded. The pulse-oximeter was adjusted in the right wrist/hand and set at maximal intensity and measurements performed every 2 seconds.

Results A total of 282 term newborn infants were included. The definitive data set comprised of 70 257 SpO_2 and 79 746 HR measurements. Median and IQR of SpO_2 (%) at 1, 5, and 10 minutes after birth were 77 (68-85), 94 (90-96), and 96 (93-98), respectively. HR (beats per minute) median and IQR at 1, 5, and 10 minutes after birth were 148 (84-170), 155 (143-167), and 151 (142-161), respectively. We found significantly higher SpO_2 for the 10th, 50th, and 90th percentiles compared with the previous reference ranges for the first 5 minutes and HR for the first 1-2 minutes after birth.

Conclusions Spontaneously breathing term newborn infants born by vaginal delivery who underwent DCC ≥60 seconds achieved higher SpO_2 and HR in the first 5 minutes after birth compared with term neonates born under the same conditions but with immediate cord clamping. Further studies in neonates undergoing cesarean delivery are under way. *(J Pediatr 2020;227:149-56)*.

The fetal life environment is relatively hypoxic compared with the extrauterine state. In the uterus, the arterial partial pressure of oxygen is 25-30 mm Hg compared with 80-90 mm Hg in the mother. The existing oxygen gradient between the mother and the fetus drives maternal-fetal gas exchange across the intervillous space of the placenta.[1] The fetal-to-neonatal transition requires a series of physiological adjustments performed in a precise sequence.[2] Immediately after birth, the onset of breathing rapidly increases the arterial partial pressure of oxygen and subsequently the availability of oxygen to the tissues.[3,4]

Cord clamping immediately after birth reduces right heart preload and pulmonary perfusion negatively influencing cardiorespiratory circulatory postnatal adaptation.[2] However, in recent years, delaying cord clamping (DCC) for around 1 minute has become a widely used clinical practice. DCC allows transferring a significant volume of placental blood to the newborn circulation that contributes to the hemodynamic stabilization and oxygenation of the newly born infant.[5,6]

Traditionally, postnatal perfusion and oxygenation have been subjectively assessed by observing the color of the newborn infant, which accounts for 20% of the Apgar score.[7] However, given the great inter- and intraobserver variability in the assessment of color even among expert neonatologists,[8] whenever a newborn baby requires resuscitation, arterial oxygen saturation (SpO_2) measured by pulse oximetry has become the standard of care in the delivery room (DR).[9] Pulse oximetry provides a continuous and reliable reading of heart rate (HR) and SpO_2 in <2 minutes.[10]

The evolution of SpO_2 and HR in the first minutes after birth has been widely studied under different circumstances such as type of delivery (vaginal or cesarean) and/or pre- or postductal readings.[3,11-24] Dawson et al built a reference range for SpO_2 and HR by retrieving these measures during the first 10 minutes after birth and using pulse oximetry in babies (308 term and 160 preterm gestation) who did not require resuscitation or oxygen after uneventful deliv-

AHA	American Heart Association
bpm	Beats per minute
DCC	Delayed (delaying) cord clamping
DR	Delivery room
ERC	European Resuscitation Council
HR	Heart rate
PI	Perfusion index
SpO_2	Arterial oxygen saturation
LMS	Licentiate in medicine and surgery

From the [1]University and Polytechnic Hospital La Fe, Valencia, Spain; [2]University of Valencia (UV), Spain; [3]Generalitat Valenciana, Consellería de Salut, Unidad Docente de Matronas, Spain; [4]Data Science Unit, Health Research Institute La Fe (IIS La Fe) Valencia, Spain; [5]Neonatal Research Group, Health Research Institute La Fe, Valencia, Spain; and [6]Nursing and Midwifery School of the Valencian Community, Spain

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eries.[3] SpO_2 IQR at 3, 5, and 10 minutes were 81% (71%-90%), 92% (83%-96%), and 97% (94%-98%) for term infants and 76% (67%-83%), 86% (80%-92%), and 94% (91%-97%) for preterm infants. Preterm infants represented 34% and very preterm <32 weeks of gestation constituted only 8% of the total. Although the majority of the babies included in this study underwent immediate cord clamping, this information was not included in the final publication.[3]

DCC and skin-to-skin contact immediately after birth has become a standard DR practice according to the 2018 guidelines of the Spanish Society for Obstetrics and Gynecology.[25] In the present study, we recorded preductal SpO_2 and HR in the first 10 minutes after birth in infants born by vaginal delivery after an uncomplicated gestation and allowed for DCC and skin-to-skin contact. Our primary objective was to build a percentile chart reflecting the physiologic oxygenation of healthy newly born infants with DCC for ≥60 seconds after birth.

Methods

Eligible infants were term newborn babies (≥37 weeks of gestation) born in the Maternity Ward of the University and Polytechnic Hospital La Fe (Valencia) after an uneventful pregnancy and vaginal delivery and not needing resuscitation or oxygen in the DR and whose parents approved participation. We defined birth as the expulsion of the entire fetal body. Babies <37 weeks of gestation, born by cesarean delivery, or needing any type of resuscitation maneuvers, with congenital malformations or chromosomopathies, not adequately monitored in the DR or with DCC for <60 seconds were excluded.

The study design was approved by the Ethics Committee of the University and Polytechnic Hospital La Fe, and parents of all the enrolled patients signed the informed consent when admitted to the Obstetric ward and before delivery took place.

The study team approached mothers with uncomplicated term pregnancies following the information received from the midwives present in the delivery suites. Mothers and fathers (if present) were informed about the study and asked for consent.

Immediately after birth, the Apgar timer was started and the pulse oximeter sensor (Masimo SET Masimo M-LNCS Neo [Low Noise Cabled Sensor], Irvine, California) was placed on the infant's right hand or wrist to get pre-ductal SpO_2 and HR. The sensor was immediately connected to the oximeter (Pulsi CO-Oximeter Radical 7 touch screen, Masimo, California).[26-28] SpO_2 and HR measurements were set at 2-second intervals and maximal sensitivity. SpO_2 sensitivity was set at ±3% for a 60%-80% SpO_2 range and HR sensitivity was set at ±3 beats per minute (bpm) for a 25-240 bpm range.[29,30] After pulse oximetry connection, newborn infants were put in a prone position on the mother's chest and covered with warm sheets and a wool cap to prevent hypothermia for at least 45 minutes. The umbilical cord was left patent for ≥60 seconds after birth. Researchers were not involved in clinical decisions or interventions. The monitor alarms were silenced to avoid interfering with the resuscitation procedures. The start-up of the Apgar timer, which coincided with complete fetal expulsion, was considered time zero for calculating time of DCC and readings of the pulse oximeter. Whenever the cord was clamped, the reading of the Apgar timer in seconds was recorded as "time of DCC" expressed in seconds. We recorded data during the first 10 minutes after birth. The data were downloaded to an individual Excel (Microsoft, Seattle, Washington) spreadsheet.

SpO_2 and HR data were stored and processed only when the signal was of good quality and in the absence of alarm messages (low perfusion, sensor off, ambient light, and low signal). We employed the perfusion index (PI) to clean the data. Thus, when the PI was <1.24, data were deleted. We employed another ad hoc designed spreadsheet to include further descriptive data from the infant, mother, and delivery (Table I).

Statistical Analyses

Data were summarized as mean (SD) and median (first, third quartile) in the case of continuous variables, and relative and absolute frequencies in the case of categorical variables.

Statistical analysis was divided into 2 parts. First, SpO_2 and HR percentiles were calculated by generalized least squares[31] regression using the rms R package (v 5.4-1R Foundation for Statistical Computing, Vienna, Austria).[32] Relevant variables such as gestational age, sex, analgesia, start (spontaneous/induced), and type of delivery (eutocic/instrumented) were introduced in the model.

We included a within-group correlation structure to correct for nonindependent observations. SpO_2 values of 100 were changed to 99.9 and then all SpO_2 values were divided by 100 so that a logit transformation could be applied. We allowed for nonlinear relationships between time (minutes) and the different response variables using natural splines. Percentiles were calculated based on the quantile function for the standard normal distribution. The estimated residual SE of each model was multiplied by the value of a standard normal distribution corresponding to the required quantile and added to the predicted mean. Logit SpO_2 percentile values were back-transformed to depict the results. Second,

Table I. Perinatal characteristics of mothers, infants, and delivery included the study

Characteristics	N = 282
Gestational age, median (range), wk	40 (37-41)
Female, n (%)	153 (54.26%)
Birth weight, mean ± SD, g	3306 ± 412
Time of DCC, mean ± SD, s	110 ± 62
Mother age, mean ± SD, y	31 (28, 35)
Labor commenced spontaneously, n (%)	179 (63.48%)
Episiotomy, n (%)	76 (26.95%)
Epidural analgesia, n (%)	232 (82.27%)
Instrumental delivery, n (%)	18 (6.38%)
First pregnancy	121 (42.91%)
Apgar score at 1 min, median (IQR)	10 (7-10)
Apgar score at 5 min, median (IQR)	10 (8-10)
Time from birth to first pulse oximetry data, median (IQR), s	62 (10-118)

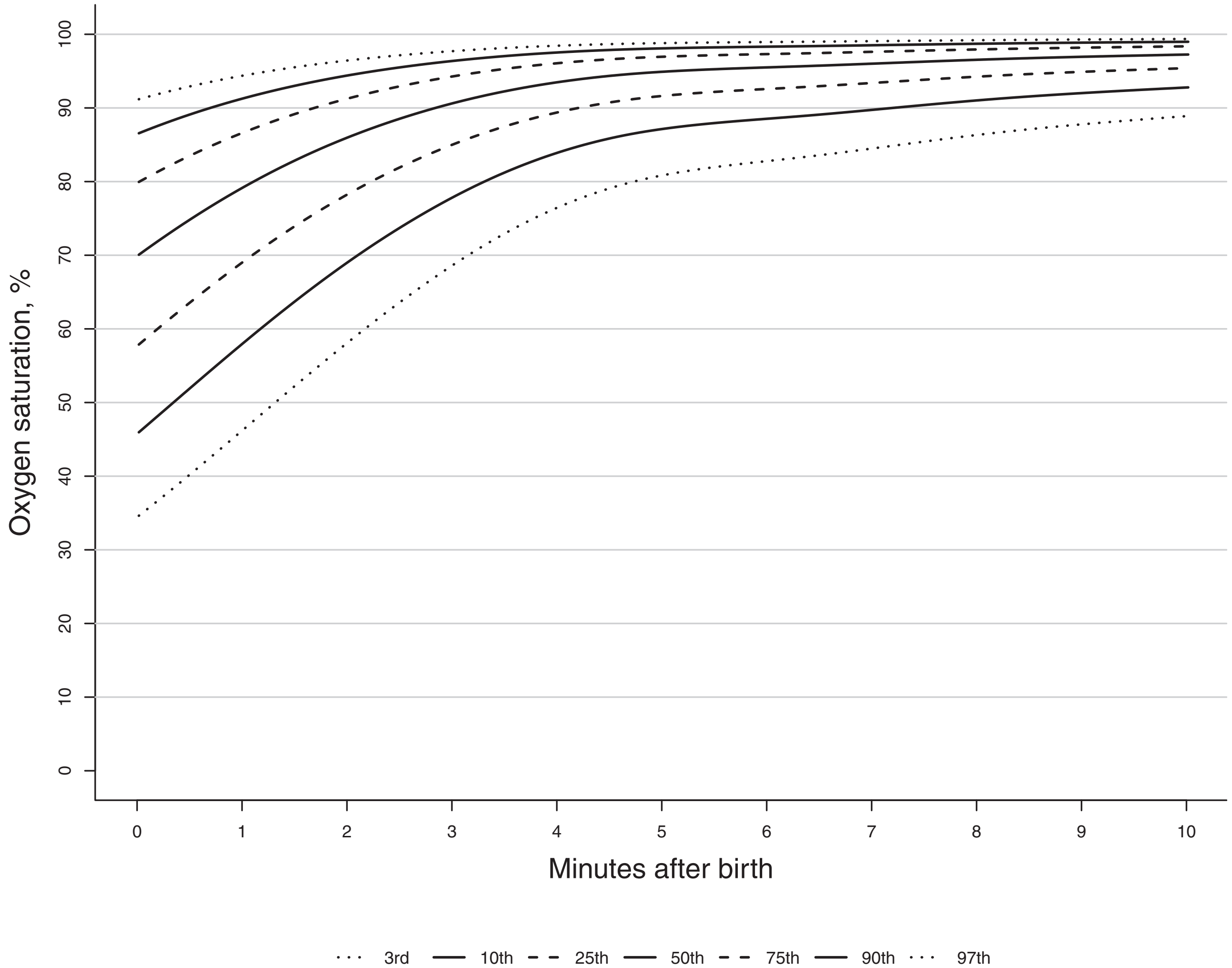

Figure 2. The graph depicts 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles of preductal SpO_2 measured with pulse oximetry in term newborn infants during the first 10 minutes with DCC for ≥60 seconds.

to perform a comparison with the percentiles from Dawson for babies born by vaginal delivery, we calculated the skewness-median-coefficient of variation (LMS) described by Cole and Green and fitted the results using the gamlss R package (v 5.1-6).[3,24,33] We used R statistical package (v 3.6.1) to perform statistical analyses.

Results

A total of 282 infants completed between July 2018 and September 2019. The final data set included 70 257 SpO_2 and 79 746 HR measurements (**Figure 1**; available at www.jpeds.com). **Table I** describes the characteristics of the infants, mothers, and delivery.

Cord clamping was delayed 110 ± 62 seconds after total fetal expulsion (**Table I**). We determined 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles for SpO_2 and HR. Results are graphically depicted in **Figures 2** and **3**. Numerical values are shown in **Tables II** and **III** (available at www.jpeds.com).

Median (IQR) of SpO_2 expressed in percentages (%) at 1, 5, and 10 minutes after birth were 77 (68-85), 94 (90-96), and 96 (93-98), respectively. Median (IQR) of HR, expressed in bpm from at 1, 5, and 10 minutes after birth were 148 (84-170), 155 (143-167), and 151 (142-161), respectively.

Tables IV and **V** show the median (IQR) for SpO_2 and HR in the first 10 minutes after birth compared with the vaginal birth group from Dawson (n = 246)[3,24] and also with the European Resuscitation Council (ERC)[34] and American Heart Association (AHA)[35] recommended target SpO_2. **Figures 4** and **5** depict the graphs with the 10th, 50th, and 90th percentiles of SpO_2 and HR in our study overlaid with the reference ranges for vaginal birth from Dawson.

Discussion

We aimed to assess a normality range for SpO_2 and HR using pulse oximetry in babies born at term after an uneventful pregnancy by vaginal delivery and with DCC for ≥60 seconds as

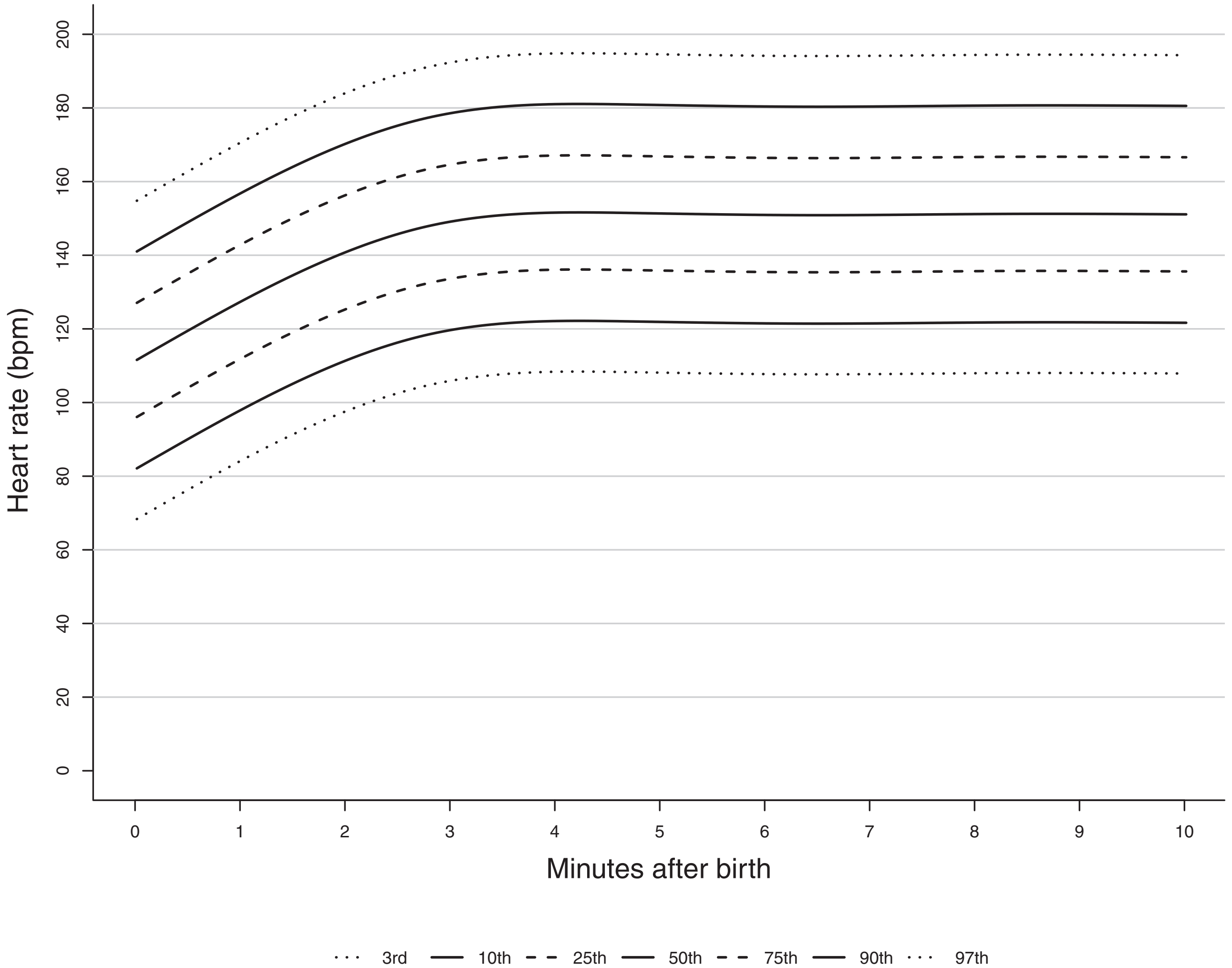

Figure 3. The graph depicts 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles of HR measured with pulse oximetry in term newborn infants during the first 10 minutes with DCC for ≥60 seconds.

presently recommended.[25] HR in the first 5 minutes after birth was accurately recorded by Linde et al, with similar results using a dry electrode EKG.[36] The cord was kept patent for more than 1 minute (110 ± 62 seconds) according to the 2018 guidelines of the Spanish Society of Obstetrics and Gynecology.[25] Normality ranges from Dawson were developed 10 years ago[3,24] when DCC was recommended. In 2015, ERC and AHA guidelines recommended DCC for 30 seconds when the baby did not need resuscitation; however, the SpO_2 ranges targeted remained unchanged.[34,35] The Dawson ranges[3] and the ERC[34] and AHA[35] target saturations stand out with substantial differences with our ranges. The 10th, 50th, and 90th SpO_2 percentiles range in our study (**Figure 4**) show significantly higher SpO_2 values in the first 5 minutes after birth than the graphs from Dawson.[3] Moreover, in **Table II**, ERC[34] and AHA[35] target SpO_2 ranges are substantially lower in each of the first 5 minutes after birth when compared with our ranges. Similarly, the 10th, 50th, and 90th percentiles for HR show less variation in our graphs when compared with those from Dawson especially in the first minutes after birth (**Figure 5**).[24] Thus, the HR in the first 2 minutes is higher in our reference range and stabilizes earlier than in the study by Dawson.[24] Because the reference ranges elaborated by Dawson et al included preterm infants and/or babies born by cesarean delivery, we also compared HR and SpO_2 median (IQR) for the 1st to the 10th minute after birth between the vaginal birth group (n = 246) in Dawson and our cohort (DCC) (**Tables II** and **III**).[3,24] SpO_2 ranges were significantly higher in the first 5 minutes after birth in our group compared with those found by Dawson.[3] We also found significant differences for HR between both ranges along the first 10 minutes.[24]

The benefits of DCC have been attributed to an increase in the circulating blood volume that would stabilize the infant's hemodynamics and contribute to preventing iron-deficient anemia.[6] Studies of the physiology of the fetal to neonatal transition in animal models have shown that DCC improves cardiovascular function and brain perfusion.[37-39] The initiation of breathing immediately after birth causes pulmonary vasodilatation and subsequently reduces pulmonary vascular resistance. The blood coming from the placenta through the patent cord increases the right ventricle preload contributing

Table IV. Preductal SpO_2, median, and IQR from the 1st to 10th minute after birth for our cohort (DCC) and the reference range in Dawson for vaginal birth

	SpO_2, median (IQR), %		
Min after birth	DCC (n = 282) Median (IQR)	Dawson vaginal birth (n = 246) Median (IQR)	*P* value
1	77 (68- 85)	67 (62-76)	<.001
2	83 (74-91)	71 (60-78)	<.001
3	90 (82-95)	80 (68-89)	<.001
4	92 (88-96)	86 (78-94)	<.001
5	94 (90-96)	92 (83-96)	.04
6	95 (91-97)	94 (87-97)	.19
7	95 (92-97)	95 (90-97)	.21
8	95 (92-98)	96 (92-98)	.45
9	96 (94-98)	96 (93-97)	.30
10	96 (93-98)	96 (93-98)	.23

Table V. HR median and IQR expressed in bpm the 1st to 10th minute after birth for our cohort (DCC) and the reference range in Dawson for vaginal birth

	HR, median (IQR), bpm		
Min after birth	DCC (n = 282) Median (IQR)	Dawson vaginal birth (n = 246) Median (IQR)	*P* value
1	148 (84-170)	99 (66-132)	<.001
2	154 (124-169)	144 (115-171)	<.001
3	157 (143-170)	160 (138-180)	<.001
4	158 (144-170)	163 (145-181)	<.001
5	155 (143-167)	164 (147-180)	<.001
6	152 (141-168)	163 (147-179)	<.001
7	153 (142-163)	162 (146-178)	<.001
8	152 (140-164)	159 (144-173)	<.001
9	152 (142-161)	157 (143-172)	<.001
10	151 (142-161)	157 (142-171)	<.001

to hemodynamic stabilization.[40,41] Prolonging the time to cord clamping positively influences the achievement of higher SpO_2 in newborn babies. Bancalari et al reported post-ductal SpO_2 and HR of 324 term newborns born by vaginal delivery and cesarean delivery subjected to cord clamping 30-60 seconds after birth.[23] The SpO_2 mean in the study by Bancalari et al for babies born by vaginal delivery at 1, 3, and 5 minutes was 62%, 75%, and 86%, whereas in our study we reported 77%, 90%, and 94% for the same timing after birth. Ashish et al randomized newborn infants ≥33 weeks of gestation to cord clamping at ≥180 seconds or ≤60 seconds after birth.[42] The main outcomes were evolving SpO_2 and HR in the first 10 minutes and time to spontaneous breathing.[42] SpO_2 was significantly higher at 1 minute (+18%), 5 minutes (+13%), and 10 minutes (+10%) in the group with patent cord ≥180 seconds. The SpO_2 values in the DCC group of Ashish et al were 79.8%, 91.2%, and 98.0% at 1, 5, and 10 minutes, similar to the values found in our study (77%, 90%, and 94%) at the same time points.[42] Anderson et al randomized late preterm and term infants born by vaginal delivery that needed respiratory support to become resuscitated with patent (>3 minutes) or early clamped cord (<1 minute).[43] The main clinical outcomes were SpO_2, HR, and Apgar score at 1, 5, and 10 minutes after birth. SpO_2 was significantly higher in the intact cord group at 1 (79.8% vs 62.4%; $P < .001$), 5 (91.4% vs 76.6%; $P < .001$), and 10 (98% vs 85.4%; $P < .001$) minutes after birth. HR was significantly higher in the early clamped group; however, in the delayed clamping group HR was >100 bpm at 1, 5, and 10 minutes.[20] International Liaison Committee on

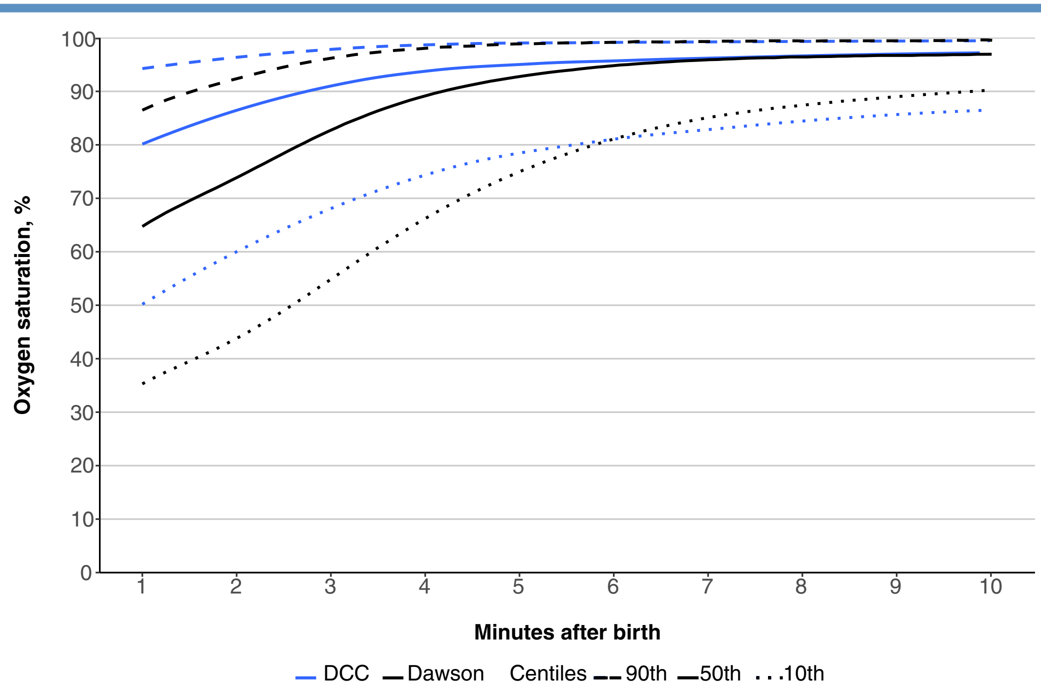

Figure 4. Comparison of the 10th, 50th, and 90th percentiles for SpO_2 measured with preductal pulse oximetry between the reference range in Dawson[3] and our study group that included DCC for ≥60 seconds.

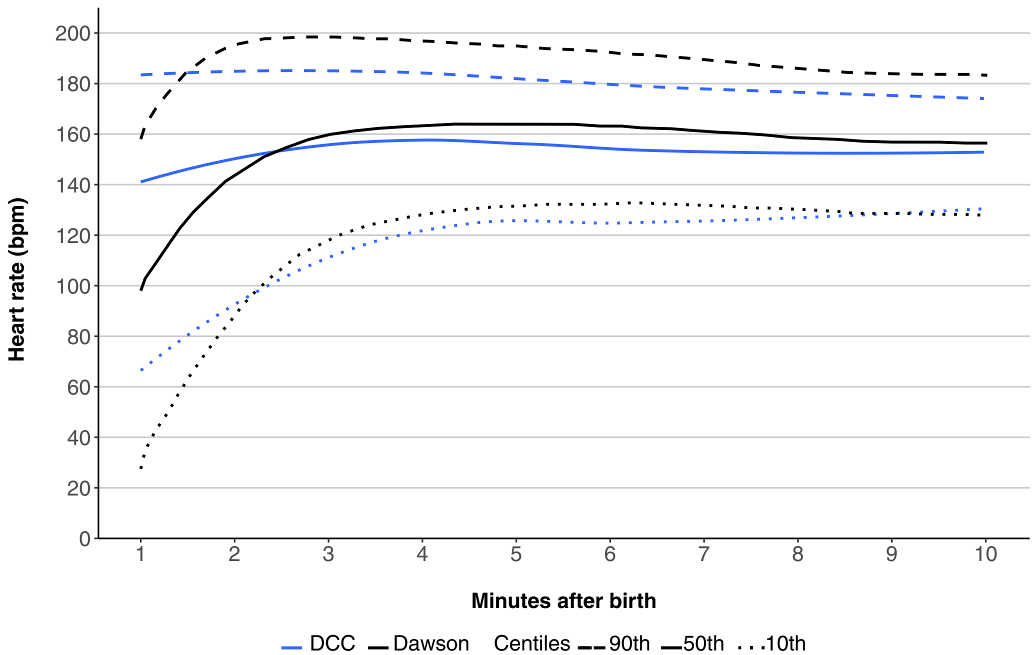

Figure 5. Comparison of the 10th, 50th, and 90th percentiles for HR measured with pulse oximetry between the reference range in Dawson[24] and our study group that included DCC for ≥60 seconds.

Resuscitation recommends in severely depressed newborn infants to clamp the cord immediately after birth and give priority to initiating resuscitation maneuvers.[44] However, experimental evidence and preliminary clinical trials convey that initiating ventilation with a patent cord while keeping the baby close to his/her mother is feasible and contributes to hemodynamic stabilization even in extremely preterm infants.[40,45,46] In this regard, several clinical trials targeting mother side stabilization of the newly born infant are ongoing. These studies include on-purpose designed devices to facilitate resuscitation with an intact cord and closeness to the mother.[47-50]

The use of pulse oximetry to monitor HR in the DR has limitations.[51] Katheria et al reported the superiority of electrocardiography compared with pulse oximetry to assess the presence of bradycardia in the first minutes after birth.[52] To minimize this limitation, we used pulse oximeters that included a filter to reject motion artifacts, set the maximum sensitivity, and increased the frequency of measurements to every 2 seconds. Thereby, we were able to capture the rapid changes of SpO_2 and HR during postnatal adaptation.[29,30] Also, to enhance the reliability of SpO_2 and HR, we employed the PI as an additional continuous noninvasive measure that evaluated hemodynamic changes. Normal values for the PI are >1.24; hence, values for SpO_2 and HR with a PI <1.24 were deleted.[53] We were sometimes limited by the difficulty of gathering the entire research group in the DR for monitoring and data retrieval. However, having a single and highly trained research group contributed to keeping up with a stringent methodological protocol and conferred homogeneity to the results.

We acknowledge limitations when comparing our results with the previous nomogram by Dawson et al.[3,24] The data provided for vaginal delivery in **Table IV** of the study by Dawson[3] included also preterm infants, whereas in our study all our babies were term infants. However, it should be underscored that very preterm babies <32 weeks of gestation included in the study by Dawson and who had the lowest initial SpO_2s, were born by cesarean delivery and, therefore, were not included in the vaginally delivered group. Thus, the vaginally delivered group in the study by Dawson only included late preterm and term infants.

DCC ≥60 seconds and early skin-to-skin contact influences preductal SpO_2 and HR during the first 10 minutes after birth. In our study, newborn infants achieved significantly higher minute-by-minute SpO_2 values in the first 5 minutes of life than the target saturations recommended by the ERC and the AHA guidelines.[34,35] Similarly, we found significantly higher values and earlier stabilization of HR in the first 2 minutes after birth than those shown in the reference range in Dawson.[24]

We conclude that DCC for more than 1 minute facilitates earlier stabilization of postnatal oxygenation and HR in the first minutes after birth in healthy term newborn infants as reflected in the updated ranges. The target ranges for SpO_2 and HR built in our study constitute a useful tool to guide resuscitation in term babies born by vaginal delivery and undergoing DCC for ≥60 seconds. Further studies for cesarean delivery with DCC are ongoing. ■

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Reprint requests: Máximo Vento, MD, PhD, Neonatal Research Group, Health Research Institute La Fe, Tower A 7th floor, Avenida Fernando Abril Martorell 106, 46026 Valencia, Spain. E-mail: maximo.vento@uv.es

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50 Years Ago in *The Journal of Pediatrics*

Umbilical Catheters—Then and Now

Krauss AN, Albert RF, Kannan MM. Contamination of umbilical catheters in the newborn infant. J Pediatr 1970;77:965-9.

With the advent of exchange transfusions, Diamond[1] introduced umbilical venous cord cannulation (UVC) in 1948. He applied Ingraham's newly developed polyethylene plastic catheter, which could be left in contact with human tissue without harm. These catheters are used for fluid resuscitation, blood sampling and transfusions, administration of intravenous medication, central venous pressure monitoring, and parenteral nutrition. In the late 1950s, cannulation of an umbilical artery became practice as well; however, it was soon evident that umbilical catheters carry risks, such as infection and embolism.

Fifty years ago, Krauss et al published a careful study examining 33 umbilical catheters (22 venous and 11 arterial) from 24 newborn infants. Positive cultures from the catheters were obtained in 57% of the infants, and there was no difference between arterial or venous catheters. Most often, the cultures showed growth of *Pseudomonas* and *Staphylococcus*. The incidence of positive cultures was not reduced by systemic antibiotics, early insertion (under 6 hours), or early removal (under 24 hours).

In a recent study, Dubbink-Verheij et al[2] detected thrombi in the umbilical venous catheter route in 75% of infants. Malposition of the catheter is quite common, and thus ultrasound confirmation of the position is recommended. In fact, despite improved techniques and catheters, the incidence rate of complications, including infections, has not decreased substantially over the last 50 years.[3]

Fifty years after the report of Krauss et al, whether prophylactic antibiotic therapy prevents catheter-related infections remains an open question.[4]

Jannicke H. Andresen, MD, PhD
Department of Neonatology
Oslo University Hospital
Oslo, Norway

Ola Didrik Saugstad, MD, PhD
Department of Pediatric Research
University of Oslo
Oslo, Norway

Ann and Robert H. Lurie Children's Hospital of Chicago
Northwestern University Feinberg School of Medicine
Chicago, Illinois

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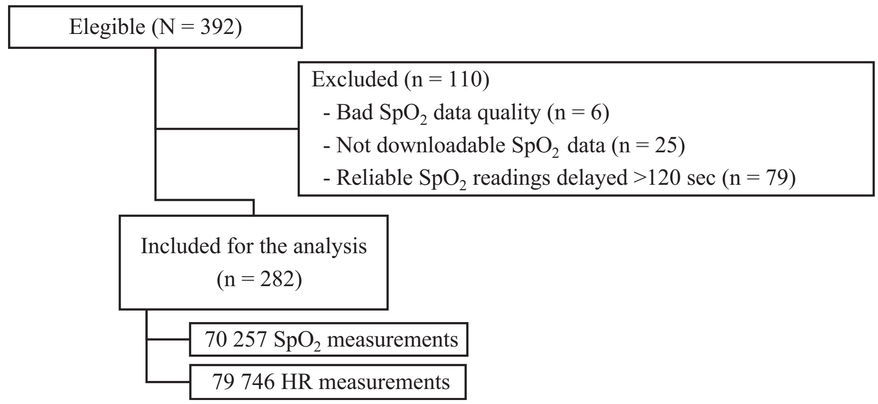

Figure 1. Flow diagram of recruitment.

Table II. Percentiles of SpO_2 (%) during the first 10 minutes of life in healthy newborn infants with DCC >60 seconds

	Percentiles of SpO_2						
Min after birth	3rd	10th	25th	50th	75th	90th	97th
1	45	58	68	77	85	92	97
2	55	66	74	83	91	97	99
3	63	75	82	90	95	98	100
4	72	81	88	92	96	98	100
5	74	85	90	94	96	98	100
6	80	86	91	95	97	99	100
7	81	88	92	95	97	99	100
8	83	88	92	95	98	99	100
9	84	90	94	96	98	99	100
10	85	89	93	96	98	99	100

Table III. Percentiles of HR expressed in bpm during the first 10 minutes of life in healthy newborn infants with DCC for >60 seconds

	Percentiles of HR						
Min after birth	3rd	10th	25th	50th	75th	90th	97th
1	45	57	84	148	170	181	188
2	52	63	124	154	169	183	190
3	46	119	143	157	170	179	193
4	66	126	144	158	170	182	196
5	82	131	143	155	167	182	193
6	73	128	141	152	168	179	192
7	114	132	142	153	163	177	191
8	107	131	140	152	164	176	187
9	122	134	142	152	161	173	188
10	92	132	142	151	161	174	190