Relation between epidural analgesia and perinatal outcomes on Robson class 2a

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BACKGROUND: : The use of epidural analgesia represents the gold standard for pain management during labor, however, the influence of the use of epidural analgesia on delivery mode and neonatal outcomes is not fully understood. Moreover, the rate of induction of labor worldwide is increasing dramatically.

OBJECTIVE: : This study aimed to analyze the impact of epidural analgesia on the mode of parturition and perinatal outcomes among individuals classified as Robson class 2a.

STUDY DESIGN: A retrospective cohort study was conducted on every Robson class 2a individual who delivered from January 1, 2022, to December 31, 2023, at the University Hospital of Modena in the north of Italy. The primary outcome was the delivery mode (cesarean delivery, vaginal delivery, and operative vaginal delivery rates), and the secondary outcomes were the effect of epidural analgesia on the duration of labor, duration of the second stage of labor, Apgar score, and neonatal intensive care unit admission.

RESULTS: Overall, 809 individuals were included in the final analysis, and 456 of them (56.4%) received epidural analgesia on request. Among individuals with and those without epidural analgesia, the cesarean delivery rate was 25% and 20.4% (P=.12), the vaginal delivery rate was 65.6% and 69.4% (P=.25), and the operative vaginal delivery rate was 9.4% and 10.2% (P=.72), respectively, without statistically significant differences. Furthermore, no significant difference was found in the neonatal outcomes between the 2 groups. Individuals with epidural analgesia had longer induction (P<.001) and second stage (P=.004) times than those without. These findings were confirmed by multivariable logistic and multinomial regression analyses. In the multivariable logistic regression, the increased induction time was associated not only with epidural analgesia (P<.001) but also with body mass index at delivery (P=.027), the gestational age at induction (P<.001), post-term pregnancy (P<.001), and induction indications of gestational diabetes or an estimated fetal weight >95th percentile (P<.001). Similarly, the increased duration of the second stage was associated not only with epidural analgesia (P=.026) but also with neonatal weight (P=.005) and induction indication for gestational diabetes or estimated fetal weight >95th percentile (P=.034).

CONCLUSION: Epidural analgesia was among the factors that increased both the induction and second stage of delivery times. However, epidural analgesia did not impact the mode of delivery and perinatal outcomes in Robson class 2a individuals.

Key words: cesarean delivery, epidural analgesia, nulliparous individuals, obstetrical anesthesia, perinatal outcomes, Robson classification

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AJOG Global Reports at a GlanceWhy was this study conducted?We conducted this study because the influence of the use of epidural analgesia on perinatal outcomes (mode of delivery and neonatal outcomes) is not fully understood, namely in Robson class 2a women (nulliparous women with induction of labor, beyond 37 weeks of gestation with a cephalic fetus).

Key findingsThere was no difference in the perinatal outcomes among women induced with and without epidural analgesia.

What does this add to what is known?Epidural analgesia was among the factors that increased both the induction and second stage of delivery times among women classified as class 2a Robson. However, epidural analgesia is not associated with an increased rate of operative deliveries or cesarean deliveries among nulliparous induced individuals. Moreover, it did not influence the neonatal outcomes.

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Introduction

Childbirth is among the most painful experiences a mother may endure, although it is included in a complex biopsychosocial network. In the absence of clinical contraindications, individuals should be offered effective pain relief. Epidural analgesia (EA) has become the gold standard for managing labor pain.[1]

The effects of EA on the progression of labor and delivery and on perinatal outcomes remain subjects of debate. However, conducting robust research on this topic is challenging because of ethical and methodologic limitations. Randomized, double-blind, placebo-controlled trials are often unfeasible, because it is neither practical nor ethical to randomize individuals to receive placebo analgesia or blind them to the insertion of an epidural catheter.[2]

Controversies persist regarding the routine use of EA, specifically in terms of its impact on labor progress and increased rates of cesarean delivery (CD) and operative vaginal delivery (OVD). The most recent Cochrane review concluded the following: "There was no difference between caesarean section rates between women with epidural analgesia and non-epidural or no pain relief during labor women (RR 1.07, 95% CI 0.96 to 1.18; 10,350 women; studies = 33; moderate-quality evidence). Although overall there appears to be an increase in assisted vaginal birth when women have epidural analgesia, a post hoc subgroup analysis showed this effect is not seen in recent studies after 2005 (Anim-Somuah et al.), suggesting that modern approaches to epidural analgesia in labour do not affect this outcome. Epidural analgesia had no impact on the risk of caesarean section or long-term backache and did not appear to have an immediate effect on neonatal status as determined by Apgar scores or in admissions to neonatal intensive care."[3]

Induction of labor has progressively increased over time and accounts for 10% to 83% of labor courses, varying with geography and parity.[4] Labor induction is also associated with increased rates of CD and OVD.[5] The effect of EA on the progress of labor has been extensively studied in individuals with spontaneous labor as opposed to induced labor. Therefore, the purpose of this study was to describe the impact of EA on delivery mode and maternal and neonatal outcomes in Robson class 2a individuals (nulliparous individuals with a single, cephalic pregnancy, at term who are undergoing labor induction) at our institution over a 2-year period.

Materials and methods

We conducted a retrospective cohort study and collected data on deliveries that occurred from January 1, 2022, to December 31, 2023, at the Mother-Infant Department of the Policlinico Hospital of Modena. The study was approved by the ethics committee of Area Vasta Emilia Nord (protocol number, 0035213/24).

Patients who met the criteria for Robson class 2a were eligible for enrollment. We included nulliparous individuals with a single, cephalic pregnancy at term who underwent labor induction, and we divided them into 2 groups, namely the analgesia group (EA), which consisted of individuals who underwent EA during labor, and the control group or non-EA group, which consistied of individuals who did not receive EA during labor. Patients who underwent a CD before the onset of labor, those who had spontaneous labor, and those with incomplete medical records were excluded.

Data were obtained from an electronic database, and they were anonymized before analysis. The population was analyzed according to the demographic characteristics (age and ethnicity), gestational weight gain (GWG), body mass index (BMI) before pregnancy, need for in vitro fertilization (IVF), gestational age at delivery, and obstetrical complications (gestational diabetes mellitus [GDM] or gestational hypertension, indication of induction of labor, method of induction, duration of induction).

As the primary outcome, we intended to assess if the mode of delivery differed among the EA and non-EA users.

As secondary outcomes we considered the time of induction to delivery mode and the duration of the second stage of labor; moreover, neonatal secondary outcomes included birth weight, Apgar score at 5 minutes, pH <7.10 or Base Excess (BE) excess of more than 12 mmol/L, and the need for neonatal intensive care unit (NICU) admission.

The duration of labor was determined by calculating the time (in minutes) from the onset of active labor to delivery.[6] The duration of the second stage of labor was determined by calculating the time (expressed in minutes) from the beginning of the pushing efforts to delivery. Augmentation with oxytocin was practiced in individuals with infrequent contractions by infusing 5 IU of oxytocin in 500 mL of lactated Ringer's solution according to the regimens prescribed by international guidelines.

The methods used for labor induction (cervical ripening balloon, dinoprostone gel, oral misoprostol, and intravenous oxytocin infusion) were decided on the basis of the Bishop score at admission.

Epidural catheters were placed at the L3 to L4 or L4 to L5 interspace, and the EA was provided with at 10 mL boluses of sufentanil and levobupivacaine 0.0625%, aiming at a walking analgesia rather than to the lowest pain score. During labor, pain was evaluated using the numeric rating scale from 0 to 10 (numerical rating scores [NRS] 0−10, with 0 = no pain and 10 = worst pain imaginable)[7]; informed consent was provided before the procedure. The data were compared for the outcomes of delivery mode, duration of labor, and duration of the second stage of labor.

Statistical analysis

The characteristics of individuals who underwent EA and the control group were analyzed and compared. In the descriptive analysis, continuous variables were summarized as mean ± standard deviation (SD), whereas categorical variables were reported as absolute and percentage values. The distribution of continuous covariates by group was compared using the 1-way analysis of variance. The comparison of categorical variables between groups was performed using the chi-square test or Fisher exact test, when appropriate. For numerical continuous variables, distributional assumptions were assessed visually using density plots and Q-Q plots. Nonparametric Wilcoxon-Mann-Whitney tests

were used for the comparisons of non-normal variables between groups. Multivariable logistic and multinomial regression analyses were used to investigate factors that were associated with mode of delivery, including the use of EA, adjusting for confounding, such as age, BMI, ethnicity, neonatal birth weight, labor duration, and the need for augmentation; candidate variables were included if they were significant in the univariate analysis or if they were clinically relevant. The results were reported as adjusted odds ratios (aOR) or adjusted relative risk ratios (aRRRs) with 95% confidence intervals (CI)s and *P* values. The statistical analyses were performed using the statistical package IBM SPSS software, version 29.0. Associations were significant at $P<.05$.

Resultes

Baseline features

A total of 809 Robson class 2 individuals were included in the final analysis. Their characteristics are summarized in the Table, stratified by the EA use (n=456 [56.4%]) and non-EA (n=353 [43.6%]) groups. Individuals in the EA group were significantly older ($P=.004$) and more frequently Italian ($P<.001$), despite having a similar prepregnancy BMI ($p = 0.85$) and the same gestational weight gain ($P=.19$). In addition, a greater proportion of individuals in the EA group had an IVFpregnancy ($P=.03$).

The prevalence of GDM and gestational hypertension was comparable between the groups.

The gestational week at the time of induction was different in the 2 groups with gestational age being later in the EA group than in the non-EA group ($P=.003$).

These findings (differences in age, nationality, IVF, and gestational age at induction, between the EA and no-EA groups) underline the complex interplay of demographic factors, clinical decisions, and cultural factors in shaping EA use. Therefore, a multivariate analysis that adjusted for these factors was conducted to limit the confounding effects.

Moreover, there were no differences in terms of medical indications for induction of labor (post-term pregnancy, GDM, or estimated fetal weight [EFW] >95th percentile). During the study period, globally, 23% of individuals underwent analgesia during childbirth.

Primary outcome

When comparing EA and non-EA users, the CD rates were respectively 25% and 20.4% ($P=.12$), the VD rates were 65.6% and 69.4% ($P=.25$), respectively, whereas the OVD rates were 9.4% and 10.2% ($P=.72$), respectively, without statistically significant differences.

We conducted a multivariable regression analysis for maternal outcomes, in particular for delivery mode (Table 1a). In this analysis, we confirmed that there was no association between the mode of delivery and the use of analgesia. Conversely, CD was significantly associated with several maternal features, such as maternal age ($P<.001$), Italian nationality ($P=.002$), IVF ($P<.001$), BMI at delivery ($P=.015$), gestational age at induction ($P=.005$), induction for post-term pregnancy ($P=.011$), and induction for EFW >95th percentile or GDM ($P=.009$). Moreover, OVD was significantly associated with other maternal factors, such as Italian nationality ($P<.001$), IVF ($P<.001$), gestational age at induction ($P=.037$), and induction for EFW >95th percentile or GDM ($P<.001$).

Secondary maternal and neonatal outcomes

Individuals who received EA experienced a significantly longer induction of labor ($P<.001$) and a longer second stage of labor ($P=.004$) than non-EA users. There were no significant differences in terms of postpartum hemorrhage, intrapartum fever, or grade 3 perineal tears (Table 2), which was confirmed in the multivariable analysis (Table 1a). No grade 4 perineal tears were found in the individuals included.

Similarly, neonatal outcomes did not differ significantly between the 2 groups (Table 3). There were no significant differences in the rate of Apgar scores ≤7 at 5 minutes, pH ≤7.10, the need for resuscitation, or NICU admission, suggesting that EA did not have adverse effects on the neonatal outcomes. Infants of mothers with EA had a significantly higher mean birth weight ($P<.001$) without a significant increase in the rate of neonatal weight >95th percentile ($P=.13$).

We classified the primary induction indication for all 809 individuals and evaluated if they were induced for post-term pregnancy or EFW > 95th percentile or GDM with no differences between the 2 groups (Table 4).

In the multivariable logistic regression (Table 1b), we identified EA ($P<.001$), BMI at delivery ($P=.027$), gestational age at induction ($P<.001$), and induction indications of post-term pregnancy ($P<.001$), GDM, and EFW >95th percentile ($P<.001$) as independent predictors of increased induction time. Moreover, a prolonged second-stage duration (Table 1c) was independently associated with EA ($P=.026$), neonatal weight ($P=.005$), and induction indication of GDM and EFW >95th percentile ($P=.034$).

Discussion

Principal findings

Our findings contribute to the ongoing debate regarding the impact of EA on delivery outcomes in induced labor. Consistent with previous studies, we observed no significant difference in the rates of CD or OVD in the EA group.[3,8,9] These findings reinforce the role of EA as a cornerstone of labor pain management in induced labor and emphasize the need for individualized approaches that balance the maternal and neonatal outcomes.

Results

Our results were in line with the previous findings of Naito et al[10] and with the conclusions of the recent Chochrane 3. However, our data were in contrast with those of Zanfini et al[11] who reported a statistically significant increase in the OVD rate across Robson classes 1 to 4 among

TABLE 1
Multivariable regression analyses.

a) Delivery mode

Delivery mode		aRRR*	95% CI	p-value
OVD	Analgesia	0.96	0.89 - 1.04	0.359
	Maternal Age	1.03	0.99 - 1.07	0.174
	Italian nationality	**0.87**	**0.83 - 0.91**	**<0.001**
	IVF	**1.39**	**1.38 - 1.4**	**<0.001**
	Neonatal weight	1.00	1.00 – 1.00	0.246
	BMI at delivery	0.98	0.93 - 1.03	0.386
	Gestational age at induction	**1.07**	**1.00 - 1.14**	**0.037**
	Induction for post term pregnancy	1.00	0.93 - 1.07	0.931
	Induction for EFW>95° or GDM	**0.66**	**0.64 - 0.68**	**<0.001**
CS	Analgesia	1.07	0.79 - 1.44	0.658
	Maternal Age	**1.09**	**1.05 - 1.12**	**<0.001**
	Italian nationality	**0.75**	**0.62 - 0.9**	**0.002**
	IVF	**1.37**	**1.32 - 1.41**	**<0.001**
	Neonatal weight	1.00	1.00 – 1.00	0.440
	BMI at delivery	**1.04**	**1.01 - 1.06**	**0.015**
	Gestational age at induction	**1.07**	**1.02 - 1.13**	**0.005**
	Induction for post term pregnancy	**1.49**	**1.10 - 2.03**	**0.011**
	Induction for EFW>95° or GDM	**1.29**	**1.06 - 1.56**	**0.009**

***RRR computed with respect to VD**

b) Time induction to labor > 24h

	aOR	**95% CI**	**p-value**
Analgesia	**2.18**	**1.57 – 3.03**	**< 0.001**
Maternal Age	0.99	0.96 – 1.02	0.556
Italian nationality	1.17	0.81 – 1.70	0.405
IVF	1.63	0.96 – 2.76	0.070
Neonatal weight	1.00	1.00 – 1.00	0.434
BMI at delivery	**1.03**	**1.00 – 1.06**	**0.027**
Gestational age at induction	**0.67**	**0.55 – 0.80**	**< 0.001**
Induction for post term pregnancy	**2.87**	**1.71 – 4.85**	**< 0.001**
Induction for EFW>95° or GDM	**2.33**	**1.48 – 3.69**	**< 0.001**

c) Duration of the second stage of labor > 2h

	aOR	**95% CI**	**p-value**
Analgesia	**1.94**	**1.10 – 3.56**	**0.026**
Age	1.04	0.99 – 1.10	0.133
Italian nationality	0.93	0.50 – 1.79	0.816
IVF	1.20	0.53 – 2.58	0.650
Neonatal weight	**1.00**	**1.00 – 1.00**	**0.005**
BMI at delivery	0.97	0.92 – 1.02	0.258
Gestational age at induction	0.99	0.73 – 1.37	0.966
Induction for post term pregnancy	0.51	0.21 – 1.17	0.119
Induction for EFW>95° or GDM	**0.36**	**0.13 – 0.86**	**0.034**

The results were reported as Adjusted Odds Ratios (aOR) and Adjusted relative Risk ratios (aRRR), with 95% confidence intervals (CI) and p-values.

CD: cesarean delivery; VD vaginal delivery; OVD: operative vaginal delivery; IVF: in vitro fertilization; BMI: Body Mass Index; GDM: gestational diabetes mellitus; EFW: estimated fetal weight

Lecis. Epidural analgesia in Robson class 2a. AJOG Glob Rep 2025.

TABLE 2
Maternal outcomes according to analgesic choice

Variables	EA (n=456; 56.4%)	NoEA (n=353; 43.6%)	Tot (n=809)	p value
CD	114 (25.0%)	72 (20.4%)	186 (23.0%)	0.12
VD	299 (65.6%)	245 (69.4%)	544 (67.2%)	0.25
OVD	43 (9.4%)	36 (10.2%)	79 (9.8%)	0.72
Time induction to labor > 24 h	**205 (46.0%)**	**102 (29.3%)**	**307 (38.7%)**	**<0.001**
Duration of the second stage of labor > 2h	**50 (12.5%)**	**18 (6.0%)**	**68 (9.7%)**	**0.004**
Postpartum hemorrhage (VD + OVD >500 mL; CD > 1000mL)	145 (31.8%)	94 (26.6%)	239 (29.5%)	0.11

Categorical variables are reported by absolute and percentage frequencies.

EA: epidural analgesia; CD: cesarean delivery; VD vaginal delivery; OVD: operative vaginal delivery

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individuals who received EA. In addition, they observed an increased risk for CD in Robson class 2a and 3 individuals with EA. These discrepancies arose despite the similar maternal characteristics between the populations studied. This outcome suggests that factors other than EA, such as physician behavior, Cardiotocography (CTG) interpretation, diagnosis of induction failure, physicians' attitudes, and non-medical influences, may play a role in the decisions regarding the mode of delivery.

When analyzing the maternal outcomes, the incidence of time from induction to delivery exceeding 24 hours was related to a combination of factors, such as the BMI at delivery, gestational age at induction, post-term pregnancy, and the induction indication of suspected macrosomia. The relationship between BMI and prolonged induction times is consistent with the results of multiple studies that indicated a prolongation of labor duration, including the time between induction and delivery, in individuals with a high BMI[12] probably because of a greater resistance to agents used for induction or other hormonal and receptorial variables that affect labor progression or because of a reduction in the intensity and frequency of uterine contractions, thereby prolonging the time it takes for cervical dilation and fetal progression.[3,13,14] In our study, the EA, together with neonatal weight and the indication for induction, was associated with a prolonged second stage of labor in nulliparous individuals who underwent labor induction. However, a longer labor duration was not associated with adverse maternal and neonatal outcomes. Our results are in line with other 2 studies[11,15] that reported that EA prolongs the second stage of labor in nulliparous (Robson 1) and multiparous individuals with and without labor induction without influencing any adverse neonatal outcomes, in accordance with this study. Indeed, the current guidelines accept a prolonged second stage of labor as a normal outcome for EA recipients with contemporary partographs allowing an additional hour for such cases.[16,17] Emerging evidence even advocates for allowing an indefinite duration if the labor progression remains safe.[11,18,19] The results of this study align with these evolving standards. Our data showed that the duration of the second stage was not only related to the presence of

TABLE 3
Neonatal outcomes according to analgesic choice.

Variables	EA (n=456; 56.4%)	NoEA (n=353; 43.6%)	Tot (n=809)	p value
Birth weight (g)	**3387±461.7**	**3240±471.7**		**< 0.001**
Birth weight > 95°centile	49 (10.7%)	27 (7.6%)	76 (9.4%)	0.13
Apgar ≤ 7 al 5'	13 (3.0%)	9 (2.7%)	22 (2.9%)	0.76
Ph ≤ 7.10	17 (4.0%)	8 (2.4%)	25 (3.3%)	0.24
Need of neonatal rianimation	7 (1.7%)	3 (0.9%)	10 (1.3%)	0.53
NICU admission	19 (4.5%)	7 (2.1%)	26 (3.5%)	0.08

Continuous variables are reported by mean and standard deviation (SD), and categorical variables as absolute and percentage frequencies.

EA: epidural analgesia; NICU: neonatal intensive care unit

Lecis. Epidural analgesia in Robson class 2a. AJOG Glob Rep 2025.

TABLE 4
Features of individuals according to analgesic choice

Variables	EA (n=456; 56.4%)	No EA (n=353; 43.6%)	Tot (n=809)	*P* value
Age (y)	32.7±5.5	31.6±5.9		.004[a]
BMI at delivery	29.2±6.4	28.5±5.4		.09
Prepregnancy BMI >30 kg/cm^2	65 (14.3%)	48 (13.8%)	113 (14.1%)	.85
Gestational weight gain at 36 wk (kg)	11.6±4.6	11.2±5.1		.19
GDM	77 (18.5%)	65 (19.9%)	142 (19.1%)	.63
Gestational hypertension	33 (7.9%)	30 (9.2%)	63 (8.5%)	.54
Italian nationality	371 (81.4%)	230 (65.2%)	601 (74.3%)	<.001[a]
In vitro fertilization	59 (12.9%)	29 (8.2%)	88 (10.9%)	.03[a]
Gestational age at induction of labor	40.0±1.1	39.7±1.2		.003[a]
Post-term pregnancy (>41+2 wk) first reason for induction	95 (20.9%)	64 (18.1%)	159 (19.7%)	.32
GDM or EFW >95th percentile first reason for induction	70 (15.4%)	53 (15.0%)	123 (15.2%)	.87
Prostaglandins as first method of induction	323 (71.3%)	256 (72.9%)	579 (72.0%)	.61
Augmentation with oxytocin	27 (8.0%)	11 (4.4%)	38 (6.5%)	.08

BMI, body mass index; *EA*, epidural analgesia; *EFW*, estimated fetal weight; *GDM*, gestational diabetes.

[a]Statistically significant.

Lecis. Epidural analgesia in Robson class 2a. AJOG Glob Rep 2025.

analgesia but also to the neonatal weight (the higher it was, the longer the expulsion period) and to the induction indication (if done for GDM or fetal weight >95th percentile); this suggests that the expulsion period is also linked to multiple factors.

Clinical implications

Regarding the neonatal outcomes, our study showed that these were unaffected in terms of acid-base status and low Apgar scores; indeed, the OVD or CD rates for fetal distress were not increased among the EA recipients. In literature, the data are controversial. The Cochrane review found no immediate adverse effects of EA on neonatal status in terms of the rate of Apgar scores <7 at 5 minutes.[3] However, a Dutch study linked EA with increased rates of low Apgar scores and NICU admissions.[20] Indeed, recent studies have suggested that combining opioids with local anesthetics enhanced analgesia while reducing the local anesthetic consumption with no reported impact on neonatal outcomes.[21] These findings underscore that modern epidural techniques are not associated with significant adverse perinatal outcomes, providing reassurance to both the providers and patients regarding the safety of neuraxial labor analgesia.

Strengths and limitation

Although this study was strengthened by rigorous methodology and the use of Robson's Ten-Group Classification System to minimize bias, certain limitations should be acknowledged. First, despite the multivariable analysis, residual confounding may have influenced the results, particularly regarding unmeasured variables such as anesthetic levels, methods of induction, and subjective pain scores. Second, variability in the clinical practices among obstetricians over the study period may have introduced inconsistencies in adherence to thresholds for assisted vaginal delivery and CD. Further clinical trials are needed to confirm our results.

Conclusion

Despite a possible prolongation of induction and labor times, EA remains a safe and acceptable practice for pain management during labor, because it is not associated with a significant increase in CD or OVD or adverse neonatal outcomes in class 2 Robson individuals.

This study underscores the importance of balancing effective pain relief with minimizing the potential adverse effects of EA on labor progression and delivery mode, namely in individuals who underwent induction of labor, which represents an increasing proportion of pregnancies. Further research, particularly prospective studies, is needed to optimize EA practices and ensure the best outcomes for both mother and baby. ■

CRediT authorship contribution statement

Serena Lecis: Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Data curation, Conceptualization. **Giulia Bonfiglioli:** Resources,

Methodology, Investigation, Data curation. **Francesco Cannistrà:** Resources, Methodology, Investigation, Data curation. **Sara Verra:** Resources, Investigation, Data curation. **Lucia Lisotti:** Resources, Investigation, Data curation. **Letizia Ramovecchi:** Resources, Investigation, Data curation. **Antonio Saddò:** Resources, Investigation, Data curation. **Giuseppe Chiossi:** Writing – review & editing. **Riccardo Cuoghi Costantini:** Formal analysis. **Roberto D'Amico:** Validation. **Sara Lazzarin:** Conceptualization. **Fabio Facchinetti:** Writing – review & editing. **Isabella Neri:** Validation. **Lara Donno:** Validation, Investigation, Conceptualization. **Massimo Girardis:** Validation. **Antonio La Marca:** Validation. **Francesca Monari:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Data curation, Conceptualization.

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