

Early PROM and Lung Hypoplasia

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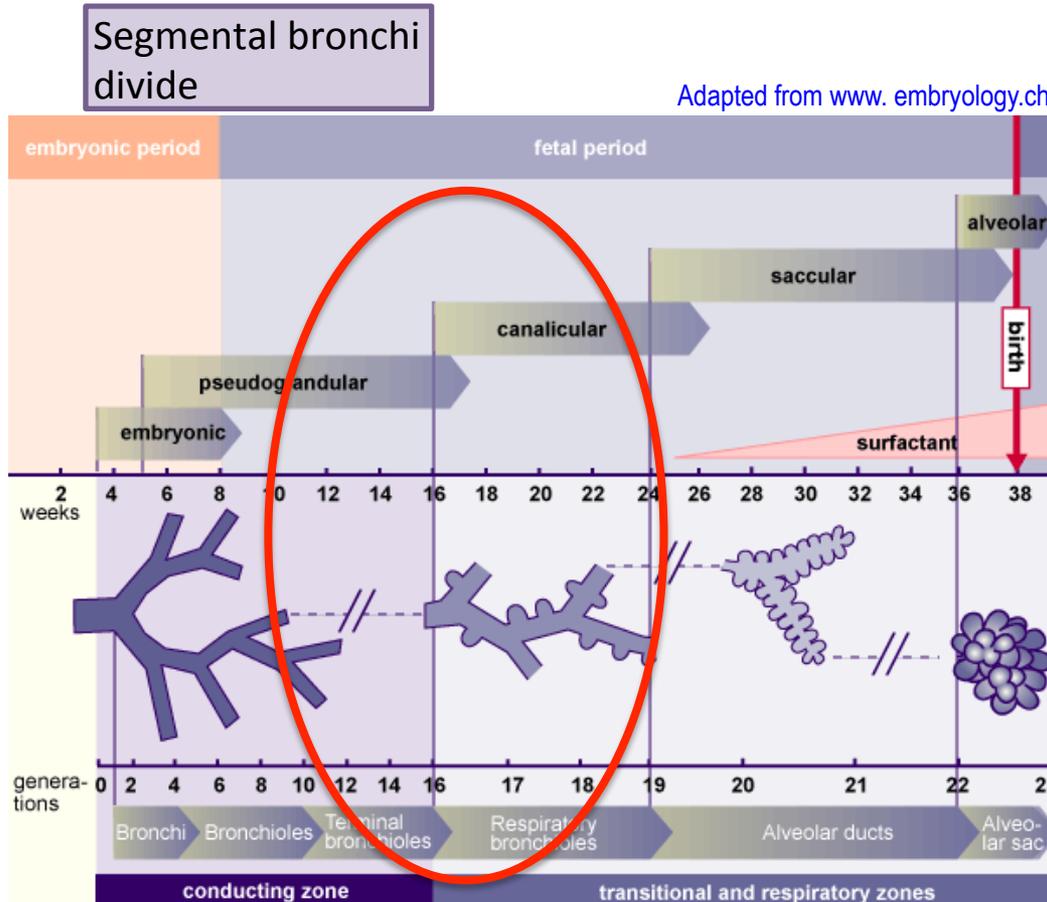
Midtrimester Preterm Rupture of the Fetal Membranes (PPROM <23 wks GA)

- Incidence: 0.4-0.7% of all pregnancies ([Waters et al. Am J Obstet Gynecol 2009;201:230](#); [Manuck et al. Am J Obstet Gynecol 2014;211:308.e1](#))
- Etiology
 - Spontaneous
 - Iatrogenic (after invasive procedures):
 - Amniocentesis: 1-2 %
 - Fetoscopy: 6-10 % ([Gratacos et al. Eur J Obstet Gynecol Reprod Biol 2000;92:151](#))
 - Operative procedures: 20-30 % ([Beck et al. Fetal Diagn Ther 2012;31:1](#))
- Counseling is complicated
 - Only small and retrospective studies available
 - Many studies before use of antibiotic prophylaxis and antenatal glucocorticoids and neonatal surfactant therapy
 - Expectant management vs. pregnancy termination?
- Latency (time interval from ROM until delivery) ([Moretti et al. 1988](#), [Taylor et al. 1984](#), [Beydoun et al. 1986](#), [Dowd et al. 1992](#), [Bentson et al. 1989](#), [Major et al. 1990](#), [Rib et al. 1993](#), [Hibbard et al. 1993](#), [Hadi et al. 1994](#), [Fortunato et al. 1994](#), [Farooqi et al. 1998](#), [Kurkinen-Raty et al. 1998](#), [Shumway et al. 1999](#), [Falk et al. 2004](#))
 - Mean latency: 17d
 - Median latency: 7d

Midtrimester Preterm Rupture of the Fetal Membranes (PPROM <23 wks GA)

- Chorioamnionitis (Moretti et al. 1988, Taylor et al. 1984, Beydoun et al. 1986, Dowd et al. 1992, Bentson et al. 1989, Major et al. 1990, Rib et al. 1993, Hibbard et al. 1993, Hadi et al. 1994, Fortunato et al. 1994, Farooqi et al. 1998, Kurkinen-Raty et al. 1998, Shumway et al. 1999)
 - 8-77% of midtrimester PPRM, 30-50% in many studies
 - More than 50% of cases during first 7d after PPRM
 - Most cases during d 2-5 after PPRM (Bedoun et al. 1986, Mc Elrath et al. 2003)
- Placental abruption: 2-44% (Hadi et al. 1994)
- Cord prolapse: 1.9% (Schucker et al. 1996)
- Fetal death:
 - Up to 33% (Dewan et al. 2001)
 - Residual amniotic fluid seems to protect against fetal death (Vergani et al. 1994)
- Stop of leakage
 - Up to 14% (Beydoun et al. 1986, Fortunato et al. 1994, Shenker et al. 1991)

Pulmonary Hypoplasia



Modifying factors

(Winn et al. *Am J Obstet Gynecol* 2000;182:1638; Vergani et al. *Am J Obstet Gynecol* 1994;170:1359)

- GA at PROM
- Duration of latency
- Residual amniotic fluid volume
 - Oligohydramnios vs. normal amniotic fluid volume: 20.9 vs. 6.7% ([Rotschild et al. Am J Obstet Gynecol](#) 1990;162;46)

- Lethal pulmonary hypoplasia rarely develops subsequent to oligohydramnios >26 wks GA ([Moessinger et al. Pediatr Res](#) 1986;20:951; [Nimrod et al. Am J Obstet Gynecol](#) 1984;148:540)
- Approx. 9-20% of newborns delivered after previable PROM will develop pulmonary hypoplasia ([Waters et al. Am J Obstet Gynecol](#) 2009;201:230)

Premature Rupture of Membranes Before Fetal Viability

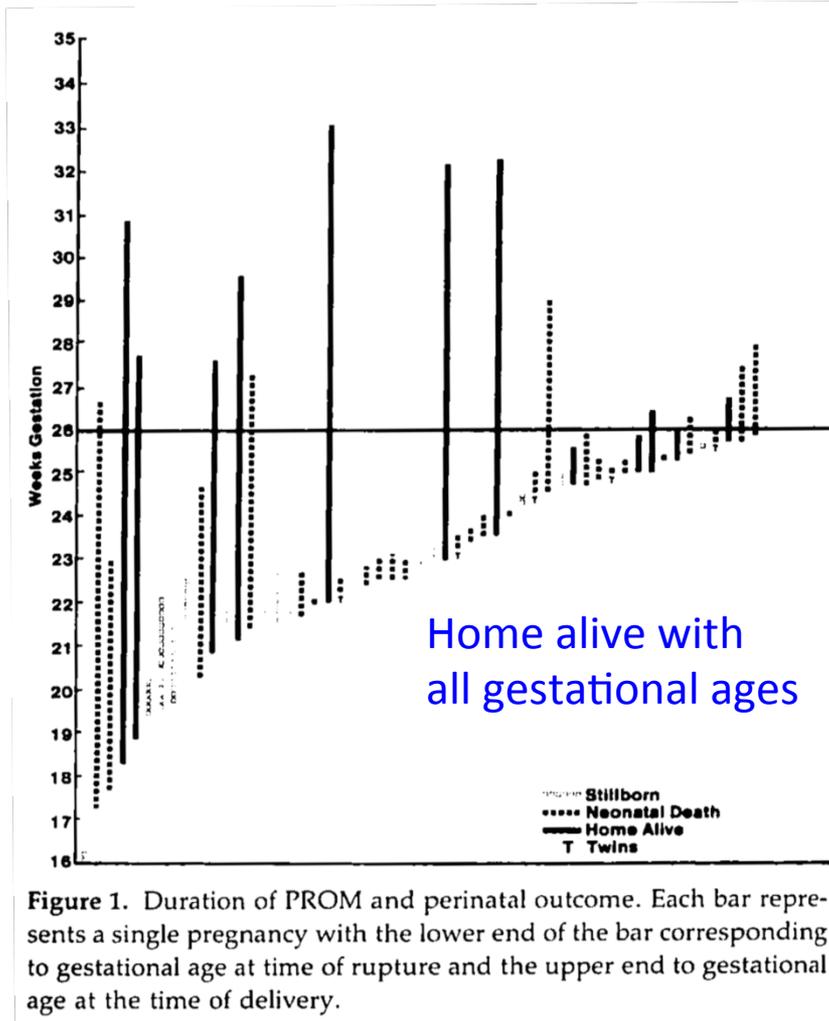


Table 2. Neonatal Morbidity With Rupture of Membranes Before 26 Weeks of Gestation

Cause of death	No. infants
Respiratory distress syndrome	8
Transient respiratory distress of the newborn	1
Pneumothorax	2
Pulmonary interstitial emphysema	2
Bronchopulmonary dysplasia	4
Intermittent apnea	6
Patent ductus arteriosus (PDA)	5
PDA requiring surgical ligation	3
Sepsis	1
Increased bilirubin	9
Necrotizing enterocolitis	2
CNS Bleed	5
Grade I	2
Grade II	1
Grade III	2
Hydrocephalus	3

Conclusions: Conservative management ...

- Maternal morbidity: 59%
- Survival 25%, with 38% of survivors normal development
- Decision of whether or not to consider conservative management should probably not be based on GA at PROM

Maternal and Perinatal Outcome of Expectant Management of Premature Rupture of Membranes in the Midtrimester

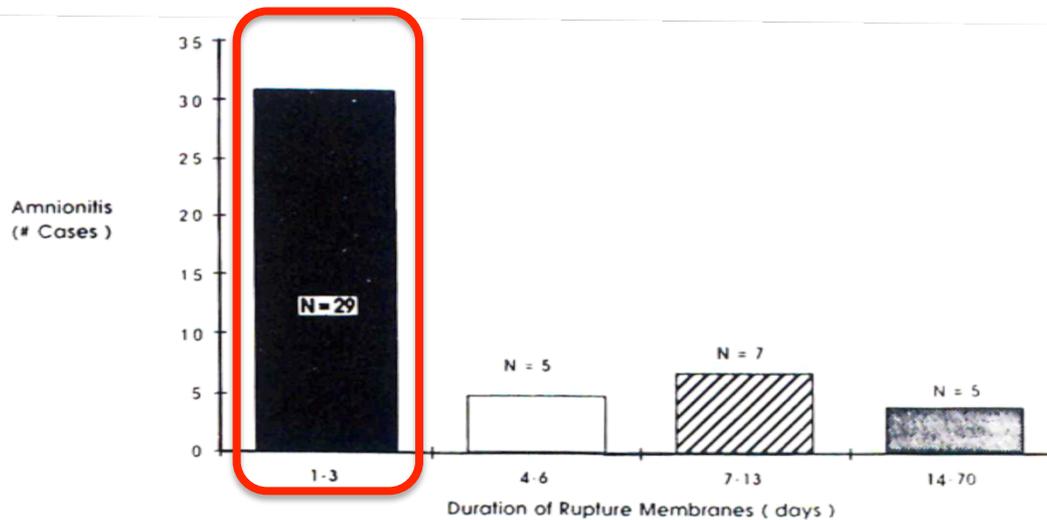


Fig. 2. Frequency of amnionitis according to latency period in days. The majority of cases of amnionitis developed within the first 3 days of rupture of membranes.

Table II. Neonatal outcome by gestational age at rupture

Completed weeks' gestation	No.	Neonatal deaths		Stillbirths	Survival	
		<24 Hr.	>24 Hr.		No.	%
16-19	16	9	3	2	2	12.0
20-22	27	17	2	6	2	7.4
23-24	35	9	11	6	9	25.0
25-26	46	4	12	3	27	58.6

Perinatal Survival with Expectant Management of Midtrimester Rupture of Membranes

GA at PPROM (wks)	No.	Stillbirth	Neonatal death	Perinatal survival	
				No.	%
19-21	6	2	0	3	50
21-23	15	5	1	10	64
23-25	25	3	9	21	64
25-26	25	1	5	21	84
TOTAL	71	11	15	45	63

- Only 1/70 infants was thought to have hypoplastic lungs
- **Conclusions:**
 - This study reveals that the neonatal outcome in patients with mid-trimester rupture of membranes is not as dismal as has been portrayed in the past
 - Expectant management of mid-trimester PROM is an reasonable option for patients as long as they are aware of their potential risks of maternal morbidity and chances of delivering a normal infant

Acute respiratory failure and short-term outcome after premature rupture of the membranes and oligohydramnios before 20 weeks of gestation

- Case-control study of all infants born after PPRM <20 wks GA (n=19) between 1990-1999, Univ. of Ulm, controls matched for year of birth, GA and BW

	PROM <20 wk (n = 19)	Control infants (n = 19)
n (%)		
Prenatal betamethasone [*]	17 (89)	12/18 (67)
Cesarean section	16 (84)	14 (74)
Gestational age [‡]	27.3 (24.4–34.0)	27.1 (24.3–34.0)
Birth weight [‡]	1020 (619–2130)	1000 (660–2080)
Small for gestational age ^{31†}	1 (5)	1 (5)
Female	11 (58)	12 (63)
Multiple gestation	5 (26)	6 (32)
[*] Two doses within 48 hours. [†] <3rd percentile. [‡] Median (minimum-maximum).		

Acute respiratory failure and short-term outcome after premature rupture of the membranes and oligohydramnios before 20 weeks of gestation

Table II. Obstetric variables and neonatal outcome of PROM in 20 infants with ≥ 24 weeks of gestation at birth

	n	CRIB score ¹⁷	RDS [†]	PPHN	CLD [*]	IVH/PVL [‡]	Survival
Gestational age at time of rupture							
14–17 wk	7	12 (5–20)	4 (57)	3 (43)	0/4	2 (29)	4 (57)
18–20 wk	13	7 (1–14)	6 (46)	4 (31)	6/10 (60)	6 (46)	10 (77)
Latency from PROM to birth							
< 9 wk	10	9 (1–12)	5 (50)	4 (40)	5/7 (71)	5 (50)	7 (70)
≥ 9 wk	10	6 (1–20)	5 (50)	3 (30)	1/7 (14)	3 (30)	7 (70)
Maximum residual amniotic fluid							
≤ 1.5 cm	10	8.5 (1–20)	6 (60)	3 (30)	3/7 (43)	4 (40)	7 (70)
1.6–3.0 cm	10	6.5 (1–14)	4 (40)	4 (40)	3/7 (43)	4 (40)	7 (70)
Year of birth							
1990–1994	8	7 (1–14)	5 (63)	2 (25)	2 (50)	4 (50)	4 (50)
1994–1999	12	7 (1–20)	5 (42)	5 (42)	4 (40)	4 (33)	10 (83)

Data are n (%) or median (minimum-maximum).
^{*}Surviving infants.
[†]RDS >grade 2.
[‡]IVH >grade 2 (all patients).

Conclusions: Expectant treatment in women with PROM20 and present neonatal intensive care has improved the survival of PROM20 infants despite severe initial respiratory failure. However, chronic morbidity still occurred.

Outcomes following prolonged preterm premature rupture of the membranes

- 2001-2005 Royal Womens Hospital Melbourne, PPRM <24 wks GA, n=98 pregnancies, 40 (41%) delivered after ≥14 d latency
- 2 L&D deaths (22, 23 wks GA), Survival rate of admitted infants: 28 (70%)

Table 1 Maternal and infant demographics

	All infants (n = 40)	Survivors (n = 28)	All deaths (n = 12)	Survivors vs all deaths
Gestation at membrane rupture, completed weeks, mean (SD)	19.8 (2.5)	20.0 (2.7)	19.4 (1.9)	p = 0.39
Latent period in days, median (interquartile range)	55 (33–77)	55 (44–82)	48 (31–71)	p = 0.44
Gestation at delivery (completed weeks), mean (SD)	28.4 (3.1)	29.3 (2.7)	26.3 (2.9)	p = 0.18
Birthweight in g, mean (SD)	1235 (557)	1357 (543)	946 (497)	p = 0.34
Male, n (%)	21 (53)	15 (53)	6 (50)	p = 0.78
Antenatal steroids, n (%)	39 (98)	28 (100)	11 (92)	p = 0.3
Histological chorioamnionitis, n (%)	24 (60)	17 (61)	7 (58)	p = 0.5

Outcomes following prolonged preterm premature rupture of the membranes

Table 2 Infant outcomes

	All infants (n = 40)	Survivors (n = 28)	Labour ward deaths (n = 2)	Neonatal unit deaths (n = 10)
1 min Apgar, median (interquartile range)	5 (2, 6)	6 (4, 7)	1 (1, 1)	2 (1, 3)
5 min Apgar, median (interquartile range)	8 (6, 8)	8 (7, 8)	1 (0, 1)	6 (4, 4)
Cord pH, median (interquartile range)		7.27 (7.23, 7.33) n = 10	–	7.22 (7.21, 7.29) n = 5
Pneumothorax, n (%)	15 (35)	7 (25)	0	8 (80)
Intubated and ventilated, n (%)	31 (78)	19 (68)	2 (100)	10 (100)
Nasal CPAP and never intubated, n (%)	5 (13)	5 (7)	–	0 (0)
Surfactant administered, n (% of those ventilated)	25 (81)	17 (89)	–	8 (80)
Chronic lung disease, n (%)	14 (35)	12 (43)	–	2 (100)*
Total duration (h) CPAP, median (interquartile range)	28 (0, 447)	112 (10, 522)	–	0 (0, 0)
HFOV				
Number of infants, n (% ventilated infants)	17 (55)	8 (29)	–	9 (90)
Total duration (h), mean (SD)	27 (0, 89)	378 (10, 71)	–	9 (2, 24)
Postnatal steroids, n (%)	3 (8)	1 (4)	–	2 (20)
Retinopathy of prematurity stage 3	1	1	–	0

*Only two infants survived beyond 36 weeks' corrected age.

CPAP, continuous positive airway pressure; HFOV, high-frequency oscillatory ventilation.

- No infant had grade 3-4 IVH or PVL
- None of the infants was discharged on O₂

- **Conclusion:** In our cohort of infants delivered following PPROM <24 wks, and treated with modern neonatal intensive care including volume-targeted and high-frequency ventilation and nitric oxide, the rate of survival to discharge is 70%.

Comparison of Perinatal Outcome After Previabable Preterm Prelabour Rupture of Membranes in Two Centres with Different Rates of Termination of Pregnancy (TOP)

(Azria et al. BJOG 2012 online 20.1.2012)

- **Methods:** retrospective comparison of perinatal outcomes in 2 French tertiary care referral centres (n= 65/77) with different rates of TOP (i.e. different approaches to management)

- **Results:**

	Center A	Center B	p
Termination of Pregnancy (TOP)	20/49 (40.8%)	36/64 (56.3%)	P<0.01
Mean latency period (d)	45.5	16.1	P<0.01
Mean GA @ delivery (wks)	28.1	25.4	P<0.01
Mean BW (g)	1295	929	P<0.01
Survival without major morbidity	42.9%	20.3%	P<0.01

- **Conclusions:** Perinatal outcomes of pregnancies managed expectantly were **not better** in the center where the **TOP rate was higher**.

The Management of Preterm Premature Rupture of the Membranes Near the Limit of Fetal Viability

(Review of the Literature published after 1994)

TABLE 2
Characteristics of pregnancies with PROM near viability

Reference	n	GA at PROM (wk)	Mean GA at PROM (SD)	Mean maternal age (y)	Antibiotics (%)	Steroids (%)	Tocolytic (%)
Xiao et al ^{11,a}	28	14–24	21.6 (2.5)	–	Yes (89.3)	Yes (75.0)	–
Grisaru-Granovsky ^{8,b}	25	16–24	22.7 (1.0)	–	Yes (88.0)	Yes (60.0)	Yes (12.0)
Falk et al ¹³	57	14–24	20.3 (n/a)	31.8 (n/a)	Yes (12.3)	Yes (33.3)	Yes (7.0)
Dinsmoor et al ^{10,c}	43	16–24	22.0 (median)	30.3 (7.0)	Yes (86.0)	Yes (n/a)	No
Muris et al ^{9,d}	49	18–24	21.1 (n/a)	29.3 (n/a)	Yes (69.4)	Yes (28.6)	Yes (14.3)
Everest et al ^{6,e}	98	<24	19.8 (2.5)	–	Yes (n/a)	Yes (97.5)	–

GA, gestational age; n/a, not applicable; PROM, premature rupture of membranes.

^a Data reported for 28 liveborn infants admitted to neonatal intensive care department; ^b Ampicillin and erythromycin were given from admission to delivery, antenatal steroids were given at 24 wk and repeated at 28 wk, indomethacin was given for tocolysis if indicated; ^c Three declined expectant management, betamethasone was given routinely at 24 wk, antibiotics were given on admission; ^d Includes 20 terminations, ampicillin given on admission, betamethasone given routinely at 22 wk and repeated weekly; ^e Data reported only for 40 liveborn with latency ≥ 14 d, erythromycin given on admission, antenatal steroids given at 24 wk.

Waters. *The management of PROM of the membranes near the limit of fetal viability. Am J Obstet Gynecol* 2009.

The Management of Preterm Premature Rupture of the Membranes Near the Limit of Fetal Viability

(Review of the Literature published after 1994)

TABLE 3

Latency after conservatively managed PROM

Reference	GA at PROM (wk)	Mean GA at PROM (wk)	Mean GA at delivery (wk)	Mean latency (d)
Xiao et al ^{11,a}	14–24	21.6 (2.5)	27.1 (2.1)	39.4 (23.9)
Grisaru-Granovsky ⁸	16–24	22.7 (1.0)	–	15.6 (n/a)
Falk et al ¹³	14–24	20.3 (n/a)	–	6.0 ^b
Dinsmoor et al ¹⁰	16–24	22.0 ^b	25.8 (3.4)	13.0 ^b
Muris et al ^{9,c}	18–24	21.1 (n/a)	23.2 (n/a)	14.1 (n/a)

GA, gestational age; n/a, not applicable; PROM, premature rupture of membranes.

^a Data reported for 28 liveborn infants admitted to neonatal intensive care department; ^b Median; ^c Outcomes for only 29 who did not terminate (n = 20) on presentation.

Waters. *The management of PROM of the membranes near the limit of fetal viability. Am J Obstet Gynecol* 2009.

The Management of Preterm Premature Rupture of the Membranes Near the Limit of Fetal Viability

(Review of the Literature published after 1994)

TABLE 4
Maternal outcomes after conservatively managed PROM

Reference	GA at PROM (wk)	n	Amnionitis, n (%)	Endometritis, n (%)	Retained placenta, n (%)	Abruption, n (%)	Sepsis, n (%)	Death, n (%)	C/S, N (%)
Taylor and Garite ¹	16–25	53	22 (41.5)	9 (17.0)	10 (18.9)	1 (1.9)	1 (1.9)	0 (0.0)	11 (20.8)
Moretti and Sibai ¹⁹	16–26	118	46 (39.3)	13 (11.0)	–	8 (6.8)	2 (1.7)	1 (0.8)	25 (21.2)
Bengston et al ³	15–26	59	27 (45.8)	4 (6.8)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	21 (36.6)
Major and Kitzmiller ⁵	19–25	70	30 (42.9)	12 (17.1)	7 (10.0)	5 (7.1)	2 (2.9)	0 (0.0)	18 (25.7)
Dowd and Permezel ⁴	17–25	71	28 (39.4)	1 (1.4)	18 (25.3)	2 (2.8)	0 (0.0)	0 (0.0)	9 (12.7)
Hibbard et al ²⁰	17–26	44	34 (77.2)	2 (4.5)	–	0 (0.0)	0 (0.0)	0 (0.0)	11 (22.9)
Morales and Talley ²¹	15–25	97	24 (24.7)	–	–	–	–	–	–
Hadi et al ⁷	20–25	178	47 (26.4)	–	–	5 (2.8)	–	–	5 (2.8)
Xiao et al ^{11,a}	14–24	28	13 (46.4)	–	–	–	–	–	13 (46.4)
Grisaru-Granovsky ^{8,a}	16–24	25	–	8 (32.0)	–	–	0 (0.0)	0 (0.0)	7 (28.0)
Falk et al ^{13,a}	14–24	57	18 (31.6)	10 (17.5)	6 (10.5)	–	0 (0.0)	0 (0.0)	11 (19.3)
Dinsmoor et al ^{10,a}	16–24	43	15 (34.9)	–	–	12 (27.9)	–	–	14 (32.6)
Yang et al ¹²	16–26	73	27 (37.0)	5 (6.8)	9 (12.3)	10 (13.7)	1 (1.4)	0 (0.0)	23 (31.5)
Muris et al ^{9,a}	18–24	49	16 (32.7)	1 (2.0)	–	5 (10.2)	1 (2.0)	0 (0.0)	–
Total		965	347/940 (36.9)	65/619 (10.5)	50/383 (13.1)	48/714 (6.7)	8/619 (1.3)	1/619 (0.2)	168/819 (20.5)
Total for studies published >1993 and with PROM ≤24 wk^a		202	62/177 (35.0)	19/131 (14.5)	6/57 (10.5)	17/92 (18.5)	1/131 (0.8)	0/131 (0.0)	45/153 (29.4)

C/S, cesarean section; GA, gestational age; PROM, premature rupture of membranes.

^a Study after 1993 with PROM ≤24 wk.

Waters. The management of PROM of the membranes near the limit of fetal viability. *Am J Obstet Gynecol* 2009.

The Management of Preterm Premature Rupture of the Membranes Near the Limit of Fetal Viability

(Review of the Literature published after 1994)

TABLE 5
Perinatal mortality after conservatively managed PROM

Reference	n	Stillbirth, n (%)	Liveborn, n (%)	Neonatal death, n (%)	Survival, n (%)
Xiao et al ¹¹	28	— ^a	—	12 (42.9)	16 (57.1)
Grisaru-Granovsky ⁸	25	—	—	17 (68.0)	8 (32.0)
Falk et al ^{13,b}	57	30 (52.6)	27 (47.4)	12 (21.1)	15 (26.3)
Dinsmoor et al ¹⁰	57	13 (22.8)	44 (77.2)	17 (29.8)	27 (47.4)
Muris et al ⁹	29	—	—	—	12 (41.4)
Everest et al ⁶	79	18 (22.8)	61 (77.2)	15 (19.0)	44 (55.7)
Total	275	61/193 (31.6)	132/193 (68.4)	73/246 (29.7)	122/275 (44.4)

PROM, premature rupture of membranes.

^a Excluded from analysis; ^b Outcomes of multiple gestation pregnancies were reported as a single outcome, with the most favorable outcome reported.

Waters. *The management of PROM of the membranes near the limit of fetal viability.* Am J Obstet Gynecol 2009.

The Management of Preterm Premature Rupture of the Membranes Near the Limit of Fetal Viability

(Review of the Literature published after 1994)

TABLE 7

Neonatal morbidity and mortality after conservative management of premature rupture of membranes near the limit of viability

Reference	n	Pulmonary hypoplasia, n (%)	RDS, n (%)	BPD, n (%)	Sepsis, n (%)	IVH grade III-IV, n (%)	ROP stage III, n (%)	NEC, n (%)	Contractures, n (%)	Hospital duration (d, mean)	Intact survival
Xiao et al ¹¹	28	7 (25.0)	12 (42.9)	8 (17.9)	5 (17.9)	1 (3.6)	–	–	–	–	10/13 ^a (76.9)
Grisaru-Granovsky ⁸	25	3 (12.0)	5 (20.0)	–	5 (20.0)	2 (8.0)	2 (8.0)	1 (4.0)	0 (0.0)	–	–
Falk et al ¹³	27	3 (11.1)	–	–	3 (11.1)	–	–	–	2 (7.4)	–	–
Dinsmoor et al ¹⁰	35 ^b	–	29 (82.9)	8 (22.9)	12 (34.3)	4 (11.4)	–	–	–	71 (median)	17/27 ^c (63.0)
Muris et al ⁹	12 ^d	–	10 (83.3)	–	5 (41.7)	0 (0.0)	–	–	0 (0.0)	27.4	–
Everest et al ⁶	40 ^e	10 (25.0)	36 (90.0)	14 (35.0)	1 (2.5)	0 (0.0)	1 (2.5)	–	–	–	–
Total	167	23/120 (19.2)	92/140 (65.7)	30/103 (29.1)	31/167 (18.6)	7/140 (5.0)	3/65 (4.6)	1/25 (4.0)	2/64 (3.1)		27/40 (67.5)

BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity.

^a Follow-up was completed by experienced pediatrician at adjusted age between 8 and 22 mo; ^b Outcomes reported for 35 liveborn resuscitated and admitted to neonatal intensive care department; ^c Ten infants with serious sequelae at time of hospital discharge;

^d Outcomes reported for 12 survivors; ^e Outcomes reported for 40 liveborn with latency of at least 14 d.

Waters. The management of PROM of the membranes near the limit of fetal viability. Am J Obstet Gynecol 2009.

The Management of Preterm Premature Rupture of the Membranes Near the Limit of Fetal Viability

(Review of the Literature published after 1994)

TABLE 9
Antenatal corticosteroids and survival

Reference	GA at PROM (wk)	n	Received steroids, n (%)	Survival with steroids, n (%)	Survival without steroids, n (%)	P
Xiao et al ^{11,a}	14–24	28	21 (75.0)	15 (71.4)	1 (14.3)	.01
Grisaru-Granovsky ^{8,b}	16–24	25	15 (60.0)	7 (46.7)	1 (10.0)	.05
Morales and Talley ^{21,c}	15–25	66	21 (31.8)	18 (85.7)	11 (31.4)	< .01
Bengston et al ^{3,d}	15–26	56	28 (50.0)	23 (82.1)	7 (25.0)	< .01

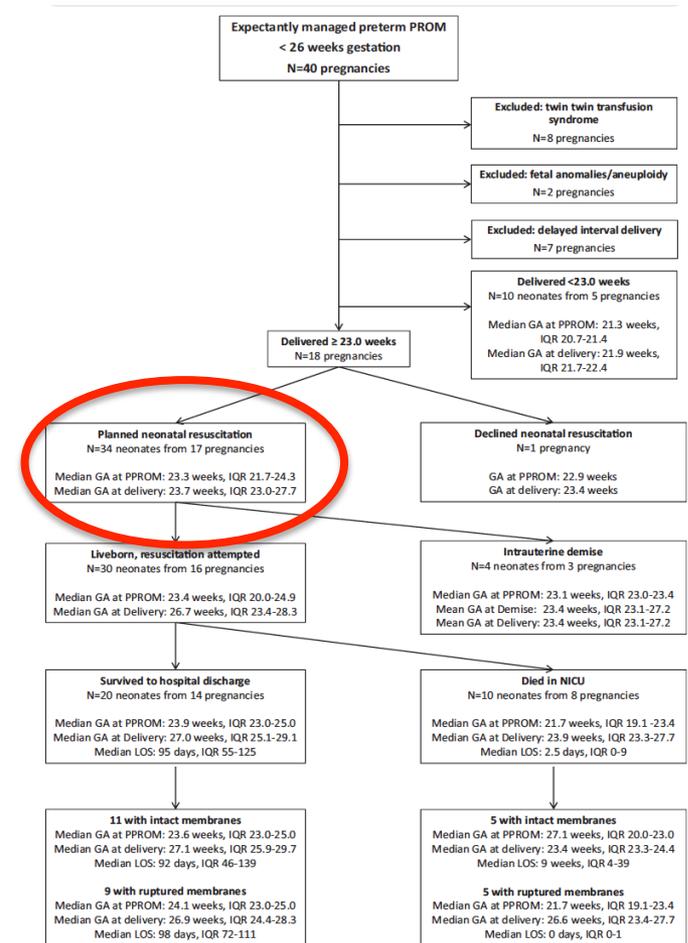
GA, gestational age; PROM, premature rupture of membranes.

^a From 1-3 courses of corticosteroids were administered at weekly or every-other-week intervals; ^b Betamethasone (2 doses of 12 mg intramuscularly at 24-h intervals) was administered at 24 wk and repeated once if delivery was considered imminent between 28-34 wk of gestation; ^c Dexamethasone (2 doses 12 mg intramuscularly at 24-h intervals) was administered at 25 wk and then weekly; ^d Dosing regimen not specified.

Waters. *The management of PROM of the membranes near the limit of fetal viability. Am J Obstet Gynecol* 2009.

Outcomes of expectantly managed pregnancies with multiple gestations and preterm premature rupture of membranes prior to 26 weeks

- Retrospective cohort study of all multi-fetal pregnancies complicated by PROM before 26 wks GA and managed expectantly
- Single institution (Salt Lake City), 4/2002-1/2013
 - 23 pregnancies/46 fetuses
 - 74% PROM <24 wks GA
 - Median latency: 11d
- 20/46 fetuses (43%) survived to hospital discharge
- 8/20 (40%) of survivors had no serious morbidity (IVH °3/4, BPD, NEC/Surgery, ROP°3-4)

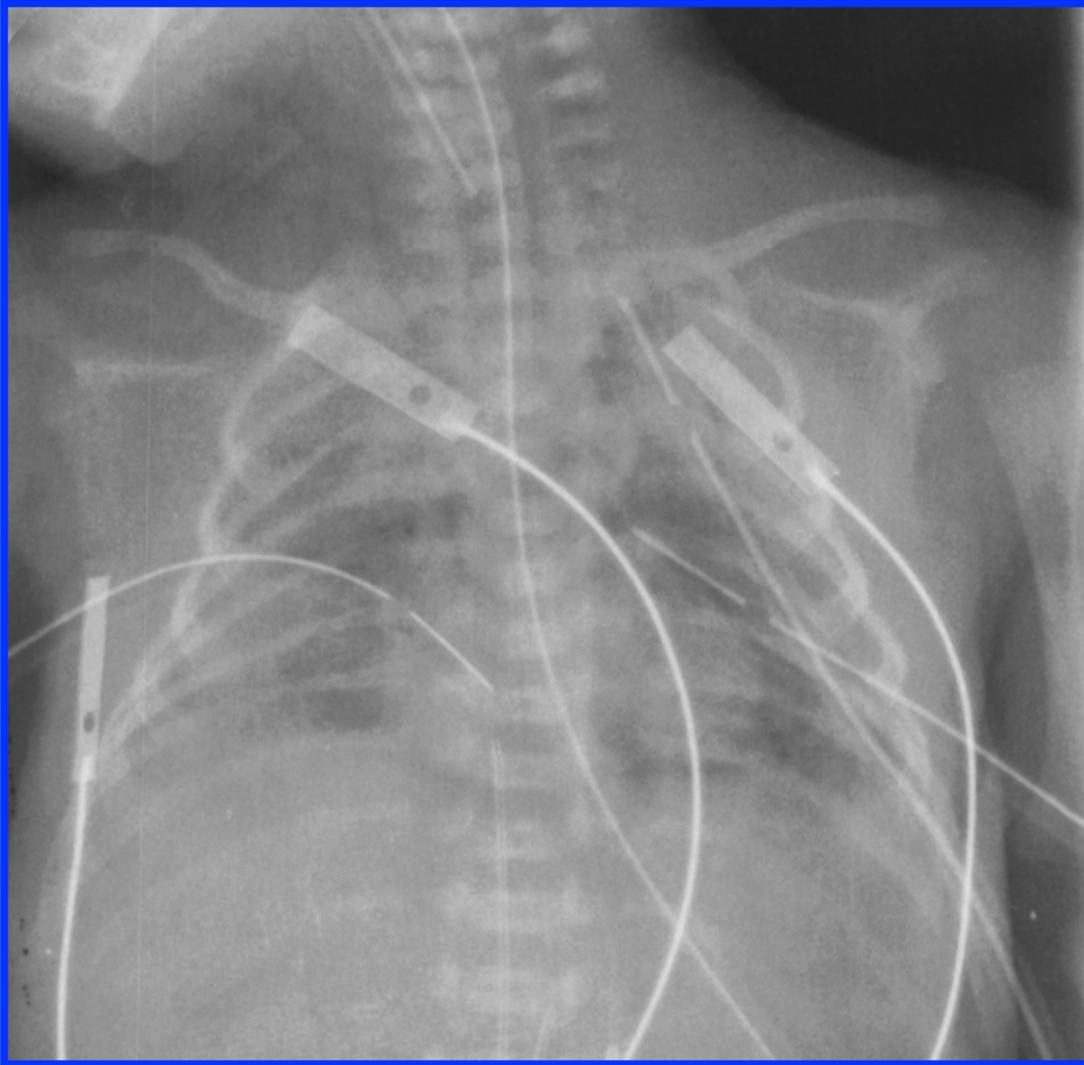


GA, gestational age; IQR, interquartile range; LOS, length of stay; NICU, neonatal intensive care unit; PPRM, preterm premature rupture of membranes; PROM, premature rupture of membranes.

Case

- PPROM with 20+3 wks GA, Oligohydramnios, Anhydramnios
- Labor with 28+2 wks GA, C/S, transverse position
- Resuscitation
 - Responding poor to non-invasive ventilation, Intubation, very little chest movement using PIP 20, 25, 30 cmH₂O
 - Surfactant, PIP up to 45 cmH₂O, no improvement, handbagging
- PTX bilat. (Transillumination): Chest tubes both sides
- Full resuscitation
- Duration of Resuscitation: 115 mins, CPR for a total time 40 mins
 - Apgar: 4(1'), 5 (5'), 5 (10')
 - worst ABG: pH 6.9, BE -19 mMol/l
- NICU Admission: 2h after birth, SpO₂ 63%, PaO₂ 35 mmHg, PCO₂ 78 mmHg, BE -15 mmol/l
 - Puncture/Drainage Pneumopericardium x 3
 - HFOV (MAP 20 cmH₂O), highest amplitude possible, iNO 20 ppm
 - IL-8 215 ng/l, CrP and Blood cultures negative

Case



- 28+3 SSW, 1180g, 2h after birth
- HFO: MAP 20cmH₂O
- Chest tubes both sides

Case

- Chest tubes d/c d 4
- HFOV until d 16, extubated d 17
- One seizure, no IVH, no PVL
- Transferred to a level 2 hospital d 41, FiO₂: 0.22-0.25
- F/U 3 years+2 months
 - Neurologically normal
 - IQ 108
- F/U 15 years
 - normal development
 - 9 th grade Middle school

Dry Lung Syndrome

- Infants with PPRM can present with severe respiratory failure immediately after birth mimicking pulmonary hypoplasia (McIntosh Arch Dis Child 1988;63:190; Blott et al. Arch Dis Child 1988;63:683; Kitterman J Pediatr 1993;123:969; Sakai et al. Acta Paediatr Jpn 1994;36:510; Losa et al. Eur J Pediatr 1998; 157:935; Nadal et al., An Pediatr (Barc) 2006;64:101, Sehgal et al. Indian J Pediatr 2010;77:1029)
 - Need for aggressive ventilatory support to survive
 - Dry lung syndrome is probably under-reported in the literature
 - Pathophysiology:
 - Compression of the airways?
 - Stiff thorax?
 - „temporary functional hypoplasia“ (McIntosh Arch Dis Child 1988;63:190)
 - May require high pressure to maintain oxygenation (HFOV has been suggested)
 - High risk for PPHN (iNO needs to be available)
- „It would seem appropriate ... to deliver these infants electively with paediatricians in attendance who are of *sufficient seniority* to assess immediately whether the normally accepted inflation pressures may need to be overridden.“ (McIntosh et al. Arch Dis Child 1988;63:190)

Transient Defect in NO Generation after Rupture of Fetal Membranes and Responsiveness to Inhaled Nitric Oxide in Very Preterm Infants with Hypoxic Respiratory Failure

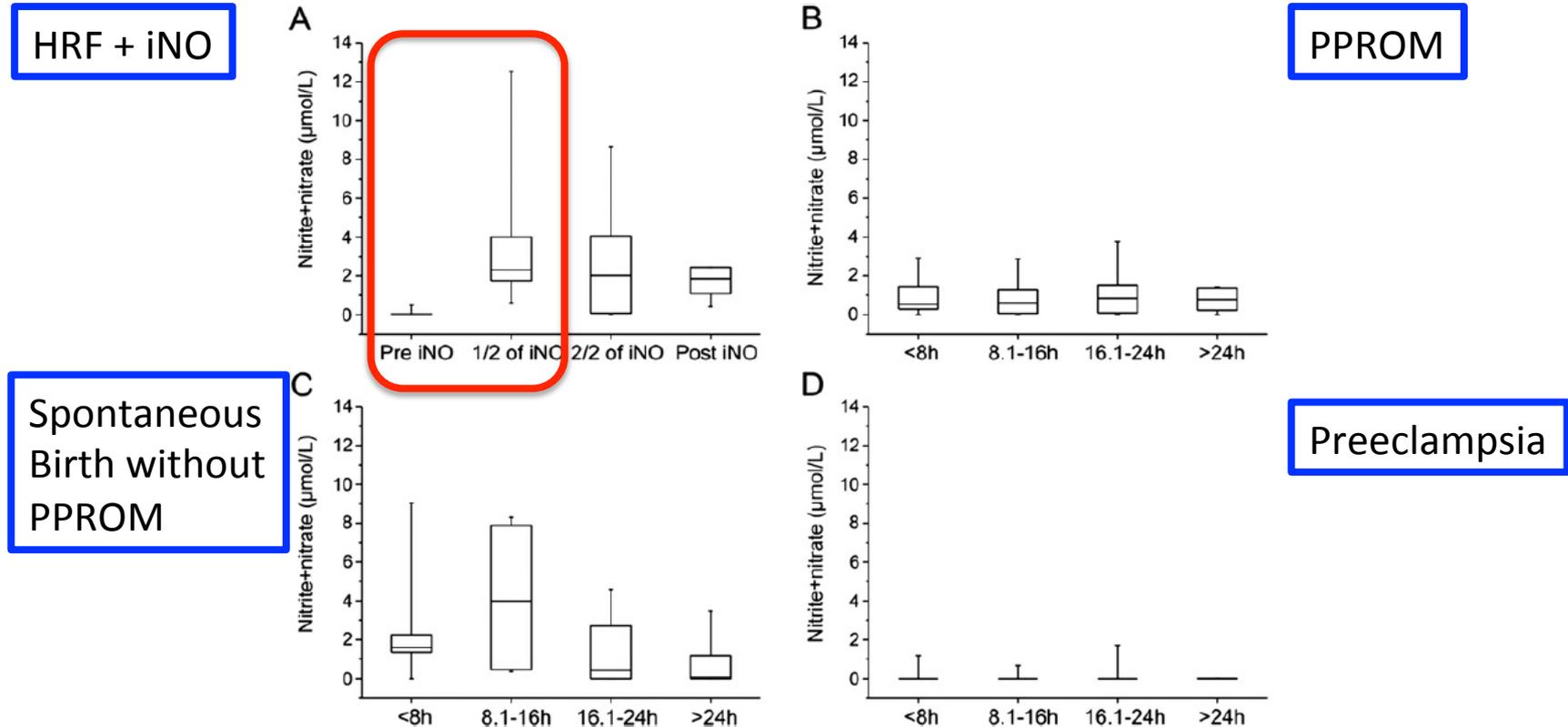


Figure 4. Box plots showing concentrations of nitrite + nitrate in airway specimens shortly after birth. **A**, HRF + iNO; **B**, PPROM; **C**, spontaneous birth without PPROM; and **D**, preeclampsia. In group A, shortly before iNO therapy, the concentration of nitrite + nitrate was lower than in group B or C. During early iNO therapy (1/2 iNO), the concentration in group A was higher than in group B. After the onset of iNO treatment, nitrite + nitrate concentrations were higher in group A than in group D ($P < .05$).

Early Functional Echocardiogram and iNO: Usefulness in Managing Neonates after PPROM

- 8 year experience using early functional echo in infants born after PPROM
- 26 infants with PPROM <20 wks GA or ROPM <25 wks GA/>14d
- 20 infants admitted to NICU
- 90% of infants admitted to NICU survived
- All infants receiving iNO survived
- **Conclusions:**
 - Premature infants with PPROM with severe hypoxic failure often have significant PPHN and may respond to HFV and iNO
 - Early echocardiography results in earlier identification and treatment

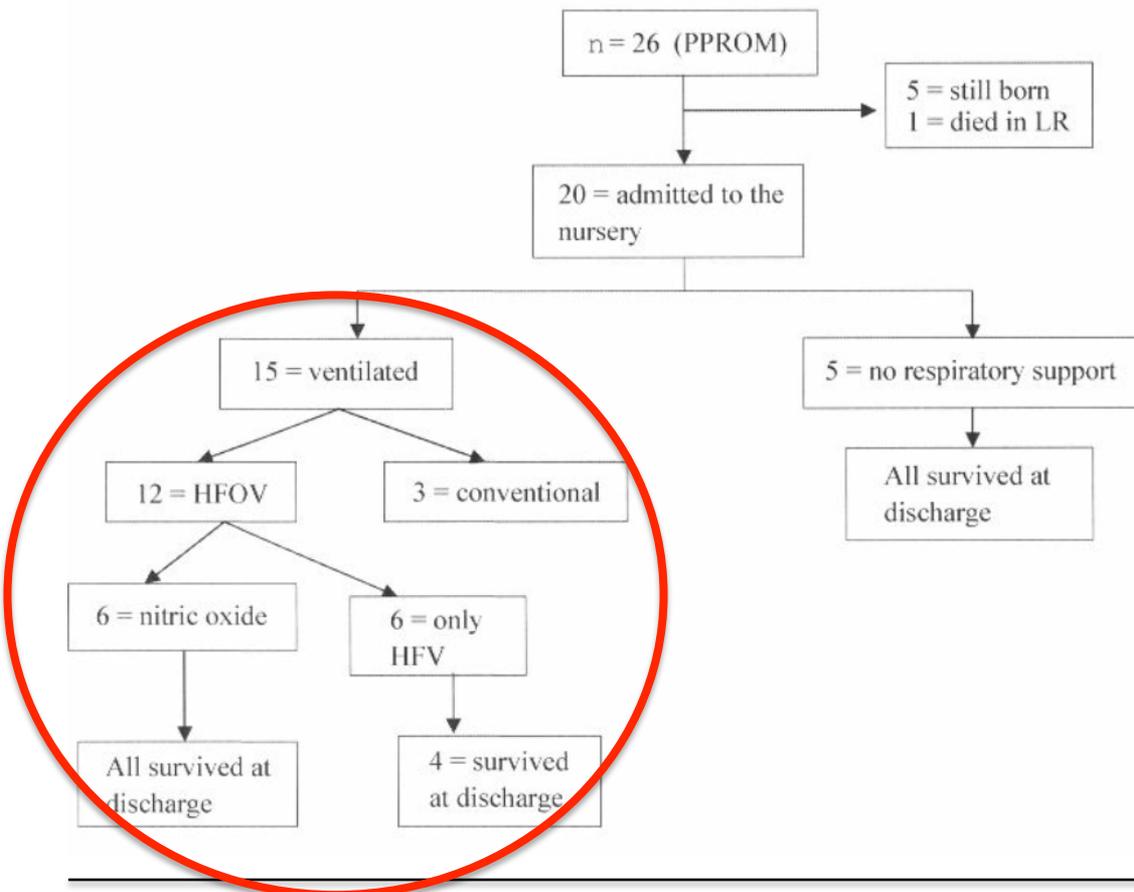


Fig. 1 Flow diagram representing all patients with preterm premature rupture of membranes (PPROM) < 24 weeks and oligohydramnios. HFV, high-frequency oscillatory ventilation.

Prolonged Rupture of Membranes and Pulmonary Hypoplasia in Very Preterm Infants: Pathophysiology and Guided Treatment

- Cardiac ultrasound scans within 2 h of life showed ...
 - a low left ventricular output due to low preload of the left ventricle,
 - a low to normal right ventricular output,
 - a normal flow in the SVC,
 - and a pure R-L-Shunt on the ductus in 6/7 infants (uncommon in respiratory disease)
- ➔ Management of infants with PPRM based on physiology (CXR + functional echocardiography)
 - ➔ Cardiac Ultrasound before and after each intervention

Prolonged Rupture of Membranes and Pulmonary Hypoplasia in Very Preterm Infants: Cardiovascular Approach

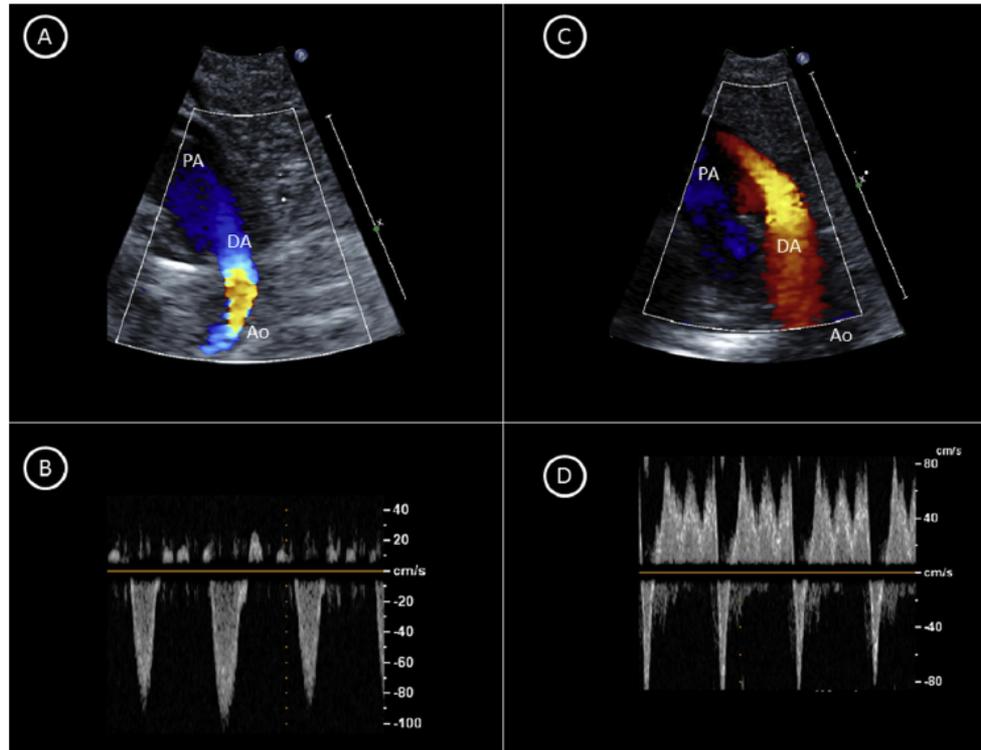


Figure 2. Left high parasternal ultrasound view of the pulmonary artery trunk (PA), ductus arteriosus (DA) and aorta (Ao) in a preterm infant with pulmonary hypertension after PPRM. **A**, Color Doppler view of pulmonary hypertension, *blue* indicating blood flowing away from the probe in all 3 vessels. **B**, Pulse-wave Doppler analysis of the waveform in the ductus arteriosus, right-to-left shunt is directed downwards. **C**, Color Doppler pattern 5 minutes after iNO was started and improved oxygenation was seen. *Red* in the ductus arteriosus indicates blood flowing towards the probe and towards the pulmonary trunk, and *blue* in the pulmonary trunk and aorta. **D**, Pulse-wave analysis now shows bidirectional flow velocity, with most of it going left-to-right, or upwards.

Prolonged Rupture of Membranes and Pulmonary Hypoplasia in Very Preterm Infants: Treatment with iNO

Table I. Summary of trials in which iNO was started early in preterm infants after PPRM in the second trimester

Study	Design	Treated with iNO	GA, wk	Ultrasound diagnosis of PH	Pre-iNO MAP, cmH ₂ O	Pre-iNO oxygenation index	Age at start iNO, h	Improved oxygenation	Survival
Peliowski et al ⁴⁰	Case series	8	24-31	5/8	12-22	25-76	2-11	8/8	5/8
Lindner et al ⁷	Case series	5	24-34	Some	n/a	n/a	n/a	4/5	n/a
Geary and Whitsett ³¹	Case report	2	29-31	1/2	n/a	n/a	10-24	2/2	2/2
Uga et al ⁴¹	Case series	8	24-30	7/8	12.6 +/- 2.8	28.8 +/- 18.3	11.5 +/- 11.6	8/8	8/8
Chock et al ⁴²	RCT	6	24-31	2/6	n/a	11-64	12 +/- 8	5/6	4/6
Williams et al ⁵	Case series	9	25-31	4/9	15-19	25-80	0.5-12	7/9	7/9
Shah and Kluckow ¹⁶	Case series	6	26-31	6/6	13-18	23-35	6-24	6/6	6/6
Welzing et al ³⁰	Case series	7	28-33	Some	n/a	n/a	0.2-15	6/6	6/6
Aikio et al ³⁹	Cohort	17	27 +/- 2	17/17	n/a	20-70	1.5-16.5	17/17	15/17

GA, gestational age; MAP, mean airway pressure; n/a, not available; PH, pulmonary hypertension; RCT, randomized controlled trial.
Data presented as range or mean +/- SD.

Improved oxygenation	63/67 (94%)
Survival	53/62 (85%)

Summary

- Chances of survival after mid-trimester PROM have improved over the last 20 years
 - If mother does not deliver within 3 d, there is a substantial chance to continue pregnancy up to many weeks
 - In the absence of acute chorioamnionitis and placental abruption expectant management is justified
- Preterm infants exposed to oligohydramnios after PROM have a higher rate of severe respiratory failure/pulmonary hypertension
- Prenatal ultrasound to detect pulmonary hypoplasia not sufficiently reliable for clinical decision making
- Risk for “true pulmonary hypoplasia” seems to be < 20% (best estimate: approx. 9%)
- Some infants exposed to PPRM may have „Dry lung syndrome“ rather than pulmonary hypoplasia
- HFV and iNO should be readily available for rescue treatment
- A targeted approach using a lung-protective ventilatory strategy and functional echocardiography seems to be useful

Thank you very much
for your attention

