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Mortality and Neurodevelopmental Outcomes in the Heart Rate Characteristics Monitoring Randomized Controlled Trial

Robert L. Schelonka, MD[1], Waldemar A. Carlo, MD[2], Charles R. Bauer, MD[3], Myriam Peralta-Carcelen, MD[2], Vivien Phillips, BSN[2], Jennifer Helderman, MD[4], Christina T. Navarrete, MD[4], J. Randall Moorman, MD[5], Douglas E. Lake, PhD[5], John Kattwinkel, MD[5], Karen D. Fairchild, MD[5], and T. Michael O'Shea, MD[6]

- **Objective:** To test whether the composite outcome of death or neurodevelopmental impairment (NDI) at 18-22 months corrected age for infants <1000 g at birth is decreased by continuous monitoring of heart rate characteristics during neonatal intensive care.
- **Study design:** subset of participants enrolled in a multicenter RCT of heart rate characteristics monitoring. Survivors were evaluated at 18-22 months corrected age with a standardized neurologic examination and the Bayley Scales of Infant Development-III (BSID-III).

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- All ELBW infants (<1000 g) in the heart rate characteristics trial enrolled at these 3 sites were eligible to participate in the current study: University of Alabama at Birmingham, Wake Forest University, and the University of Miami.

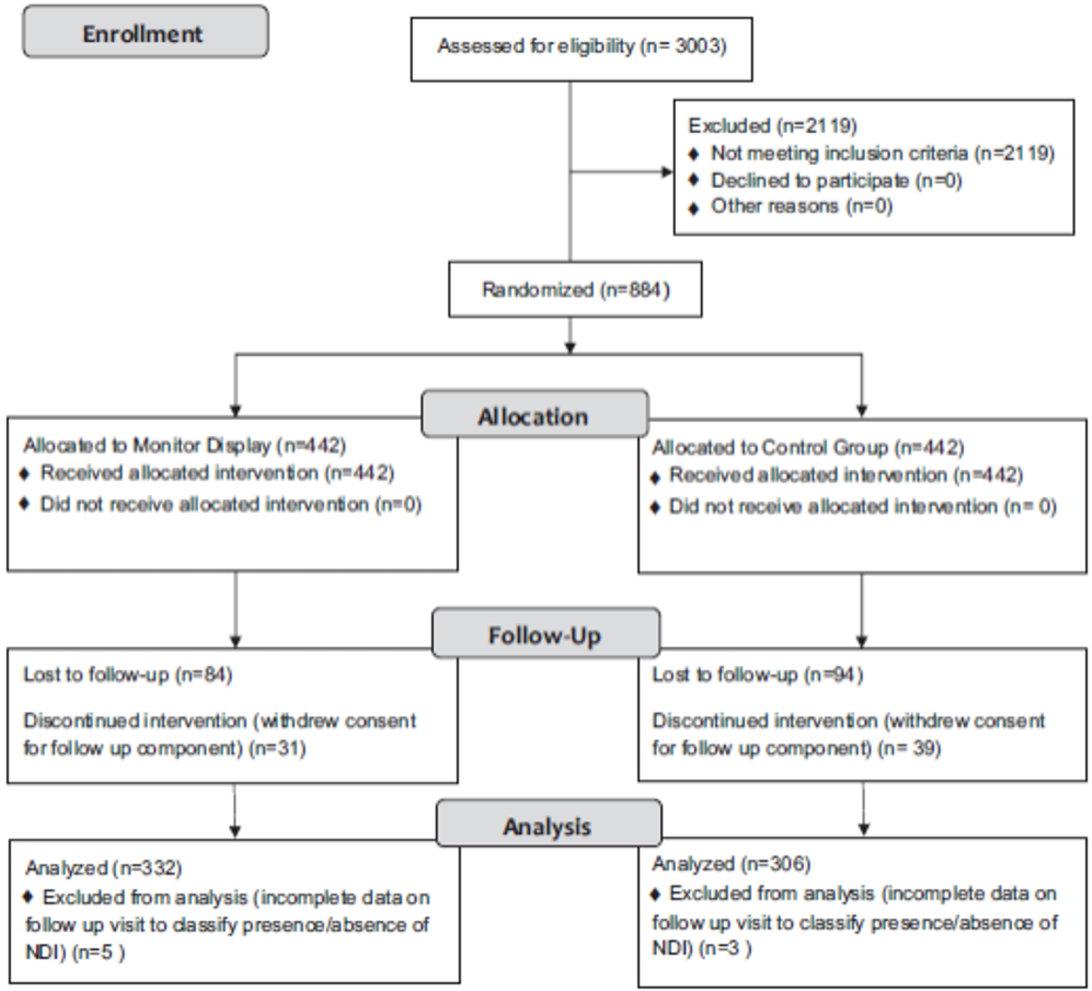
Enrollment
Assessed for eligibility (n= 3003)
Excluded (n=2119)
♦ Not meeting inclusion criteria (n=2119)
♦ Declined to participate (n=0)
♦ Other reasons (n=0)
Randomized (n=884)
Allocation
Allocated to Monitor Display (n=442)
♦ Received allocated intervention (n=442)
♦ Did not receive allocated intervention (n=0)
Allocated to Control Group (n=442)
♦ Received allocated intervention (n=442)
♦ Did not receive allocated intervention (n= 0)
Follow-Up
Lost to follow-up (n=84)
Discontinued intervention (withdrew consent for follow up component) (n=31)
Lost to follow-up (n=94)
Discontinued intervention (withdrew consent for follow up component) (n= 39)
Analysis
Analyzed (n=332)
♦ Excluded from analysis (incomplete data on follow up visit to classify presence/absence of NDI) (n=5)
Analyzed (n=306)
♦ Excluded from analysis (incomplete data on follow up visit to classify presence/absence of NDI) (n=3)

Table I. Characteristics of the infants with outcome known and not known according to monitoring assignment

Variables	Outcome known: Display (n = 322)	Outcome known: Control (n = 306)	*P* value 1	Outcome not known: Display (n = 120)	Outcome not known: Control (n = 136)	*P* value 1	Comparison *P* value 2
Baseline							
Birth weight, g	746 ± 154	723 ± 152	.05	811 ± 140	779 ± 148	.07	.0001
Gestational age, wk	26 ± 2.1	26 ± 1.9	.3	27 ± 2.1	27 ± 2.1	.11	.0001
Male	172 (53.4)	153 (50.0)	.42	59 (49.2)	57 (41.9)	.26	.08
Maternal chorioamnionitis	37 (11.5)	37 (12.1)	.9	10 (8.3)	17 (12.5)	.31	.64
Antenatal steroids	256 (79.5)	239 (78.1)	.69	83 (69.2)	98 (72.1)	.68	.01
Neonatal outcomes*							
Apgar at 5 min of <7	112/319 (37.1)	118/302 (37.0)	1.0	38 (32.2)	46 (34.9)	.69	.35
Culture-proven sepsis	130/322 (40.4)	131/306 (42.8)	.57	42/120 (35.0)	49/136 (36.0)	.89	.11

Values are mean ± SD or number (%).
*Total number refers to the number of infants assessed for the outcome if different from the number in that group.

- Death or NDI, the primary composite outcome, was known in 322 infants (73%) in the monitor display group and 306 infants (69%) in the control group.
- Infants in the monitor display group were on average 23 g heavier at birth than the control group (746 154 g vs 723 152 g; P = .05).

Table II. Mortality and neurodevelopmental findings at 18-22 months according to treatment assignment

Variables	Display	Control	RR (95% CI)	*P* value
Primary outcome				
Death or NDI	127/321 (39.6)	136/306 (44.4)	0.89 (0.74-1.07)	.223
Death	79/327 (24.2)	99/309 (32.0)	0.75 (0.59-0.97)	.028
Death or the following specific components of NDI				
GMFCS level 2-5 (moderate/severe CP)	127/321 (39.6)	136/306 (44.4)	0.89 (0.74-1.07)	.223
Bilateral blindness	83/326 (25.5)	99/309 (32.0)	0.79 (0.62-1.02)	.079
Deafness	90/327 (27.5)	100/309 (32.4)	0.85 (0.67-1.08)	.194
Bayley cognitive <70	102/322 (31.7)	113/306 (36.9)	0.86 (0.69-1.07)	.179
Bayley language <70	115/320 (35.9)	127/305 (41.6)	0.86 (0.71-1.05)	.163
NDI and specific components of NDI, survivors only				
NDI	53/247 (21.5)	40/210 (19.1)	1.12 (0.78-1.63)	.561
GMFCS level 2-5 (moderate/severe CP)	23/246 (9.4)	13/210 (6.2)	1.51 (0.78-2.9)	.223
Bilateral blindness	4/247 (1.6)	0/210 (0)	0 (0-0)	.128
Deafness	11/248 (4.4)	1/210 (0.5)	9.31 (1.21-71.55)	.008
Bayley cognitive <70	23/243 (9.5)	15/207 (7.3)	1.31 (0.70-2.43)	.497
Bayley language <70	36/241 (14.9)	28/206 (13.6)	1.01 (0.69-1.74)	.787

Values are number/total number (%).
NDI is a GMFCS level of 2-5 (moderate/severe CP, blind, deaf, language or cognitive Bayley score <70). The RR is of the outcome in the display group as compared with the control group.

- The proportion with death or NDI did not differ between groups.
- Death was decreased from 32.0% (99/309) for infants in the control group to 24.2% (79/327) in the monitor display group.
- Infants who were blind and who had abnormal neurologic examination did not significantly differ.
- More infants in the display group were deaf: 11 in 248 (4.4%) vs 1 in 210 (0.5%; P = .008).

Table III. Mortality and additional neurodevelopmental findings at 18-22 months according to treatment assignment

Death or the following neurodevelopmental outcomes	Display	Control	RR (95% CI)	*P* value
GMFCS level 1 (mild CP)	114/325 (35.1)	134/309 (43.4)	0.81 (0.67-0.98)	.035
GMFCS level 2-3 (moderate CP)	96/325 (29.5)	107/309 (34.6)	0.85 (0.68-1.07)	.174
GMFCS level 4-5 (severe CP)	85/325 (26.2)	104/309 (33.7)	0.78 (0.61-0.99)	.046
Bayley cognitive 70 – 84	106/321 (33.0)	125/306 (40.8)	0.81 (0.66-0.99)	.047
Bayley language 70 – 84	148/320 (46.3)	164/306 (53.6)	0.86 (0.74-1.01)	.079

Values are number/total number (%).
The RR is of the outcome in the display group as compared with the control group.

- Fewer infants in the display group than those in the control group had:
  - death or mild CP (114/325 [35.1%] vs 134/309 [43.4%]; P = .035),
  - severe CP (85/325 [26.2%] vs 104/309 [33.7%]; P = .046),
  - Bayley cognitive scores of 70-84 (106/321 [33.0%] vs 125/306 [40.8%]; P = .047.

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- **Conclusion:** We found no difference in the composite outcome of death or NDI for extremely preterm infants whose heart rate characteristics were and were not displayed during neonatal intensive care.
- Two outcomes that included mortality or a specific NDI were less frequent in the displayed group.

Trends in Breastfeeding Interventions, Skin-to-Skin Care, and Sudden Infant Death in the First 6 Days after Birth

Melissa Bartick, MD, MSc, FABM[1], Mary Ellen Boisvert, MSN, CLC, CLE[2,*], Barbara L. Philipp, MD, FAAP, FABM[3], and Lori Feldman-Winter, MD, MPH, FAAP, FABM[4]

- **Objective:** To determine if implementation of skin-to-skin care and the Baby-Friendly Hospital Initiative (BFHI) contributes to sudden unexpected infant death (SUID) and asphyxia in the first 6 days after birth.
- **Study design:** survey data to determine a correlation between BFHI and deaths from SUID and asphyxia among infants <7 days in the US and Massachusetts. Using data from the CDC, implementation of BFHI was tracked from 2004-2016 and skin-to-skin care was tracked from 2007-2015. Using data from CDC and the Massachusetts Department of Public Health, SUID and asphyxia were tracked from 2004-2016.

TEN STEPS TO SUCCESSFUL BREASTFEEDING
(JOINT WHO/UNICEF STATEMENT, 1989)

1. Have a written breastfeeding policy that is routinely communicated to all health care staff.
2. Train all health care staff in skills necessary to implement this policy.
3. Inform all pregnant women about the benefits and management of breastfeeding.
4. Help mothers initiate breastfeeding within a half-hour of birth.
5. Show mothers how to breastfeed, and how to maintain lactation even if they should be separated from their infants.
6. Give newborn infants no food or drink other than breastmilk unless medically indicated.
7. Practice rooming-in -allow mothers and infants to remain together -24 hours a day.
8. Encourage breastfeeding of demand.
9. Give no artificial teats or pacifiers (soothers, dummies) to breastfeeding infants.
10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic.

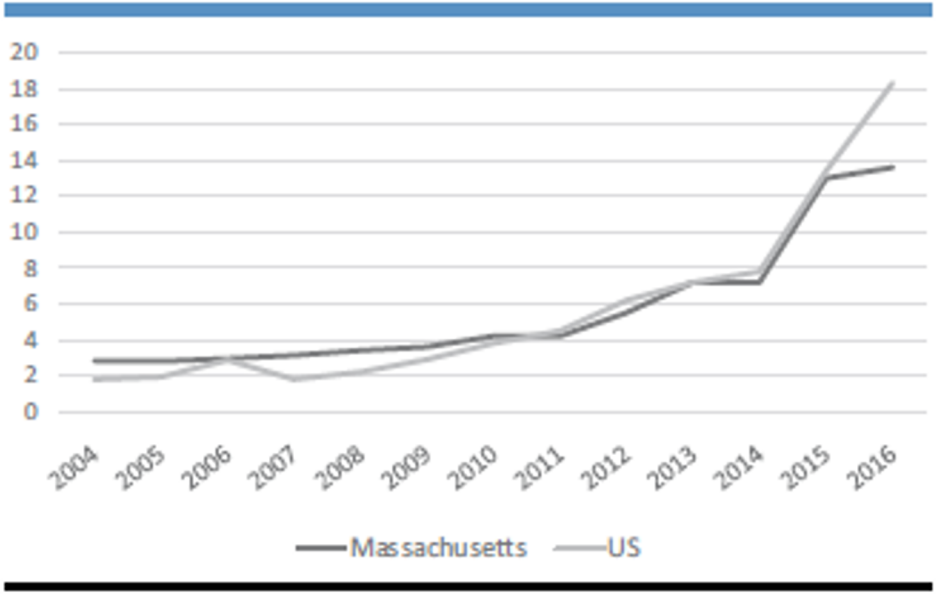

Figure 1. Percentage of births in Baby-Friendly facilities, 2004-2016.

- Nationally, the percentage of births in Baby-Friendly facilities rose from 1.8% in 2004 to 18.3% in 2016.
- In Massachusetts, the percentage of births in Baby-Friendly facilities grew from 2.8% in 2004 to 13.6% in 2016.

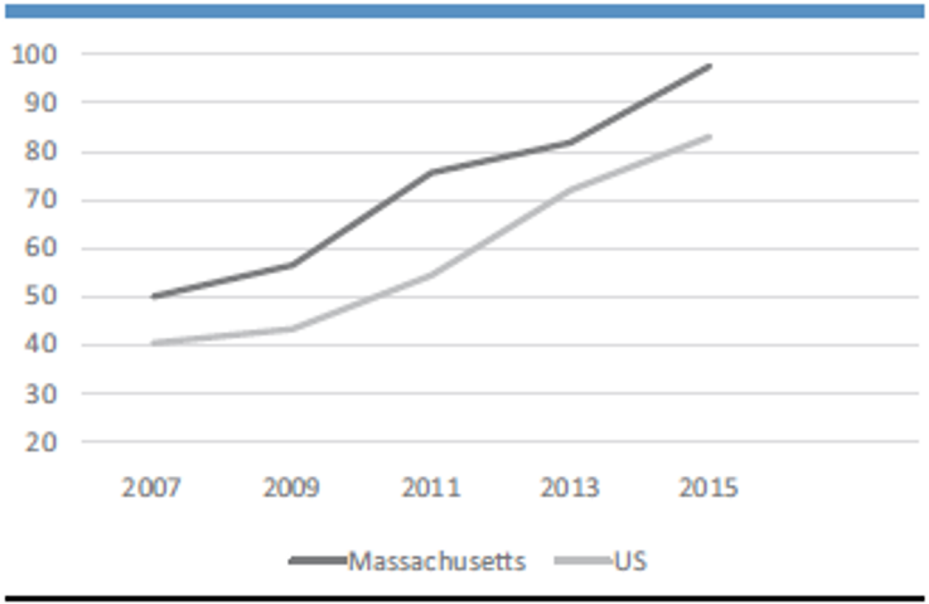

Figure 2. Percentage of maternity facilities in which most dyads experience skin-to-skin care in the first hour.

- The percentage of hospitals where “most” mother-infants pairs experienced skin-to-skin contact for at least 30 minutes within 1 hour of an uncomplicated vaginal birth rose:
  Nationally: from 40.4% in 2007 to 83.0% in 2015.
  Massachusetts: from 50% in 2007 steadily to 97.8% in 2015.

Table. SUID prevalence characteristics, infants <7 days of age, US and Massachusetts, 2004-2016

	2004-2009	2010-2016	OR 2010-2016 compared with 2004-2009	95% CI
US SUID prevalence	0.033	0.028	0.85	(0.77, 0.94)
US ASSB prevalence	0.002	0.003	1.41	(1.02, 1.94)
US preterm SUID prevalence	0.014	0.011	0.74	(0.64, 0.87)
% SUID that are preterm, US	43.7%	38.0%	0.74	(0.64, 0.87)
%. SUID are non-Hispanic white, US (% of US births that are non-Hispanic white)	52.7% (54.2%)	53.3% (46.2%)	1.17	(0.96, 1.42)
% SUID are non-Hispanic black US (% of US births that are non-Hispanic Black)	39.0% (14.4%)	21.8% (14.8%)	0.56	(0.45,0.69)
SUID prevalence non-Hispanic white	0.030	0.032	1.08	(0.94, 1.24)
SUID prevalence non-Hispanic Black	0.089	0.036	0.40	(0.34, 0.49)
MA SUID prevalence	unreliable	unreliable	0.32	(0.13, 0.82)
MA ASSB prevalence	0	0	0	Not applicable

Prevalence is noted as "unreliable" if the numerator is <20, making a calculation of prevalence unreliably precise by CDC standards. Prevalence rates are per 1000 live births.

- The SUID prevalence decreased between the 2 study periods.
- Overall from 2004-2016, 40.1% of national SUID deaths were in preterm infants.
- A disproportionately high percentage of SUID deaths during the first 6 days after birth were in non-Hispanic black infants, although this dropped markedly during the study period.

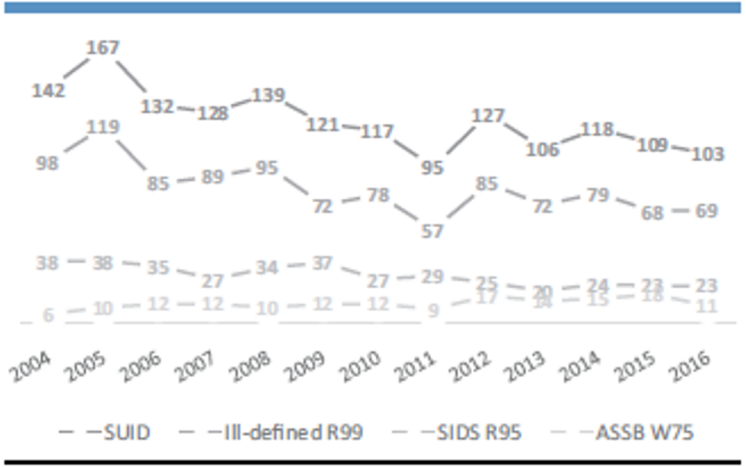

Figure 3. Trends in US deaths per year among infants <7 days of age, 2004-2016. Total deaths are shown rather than prevalence because of the very low numbers of ASSB deaths, preventing a reliably precise calculation. Total births increased from 4 112 055 in 2004 to 4 316 213 in 2007, then declined to 3 945 875 in 2016.

- Only 0.72% of neonatal deaths from 2004-2016 were due to SUID in infants in the first 6 days after birth.
- The total number of Massachusetts SUID deaths within 6 days after birth over this 13-year period is very small (n = 22). There were zero ASSB deaths during this 13-year period.

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- **Conclusion:** Increasing rates of breastfeeding initiatives and skin-to-skin care are temporally associated with decreasing SUID prevalence in the first 6 days after birth in the US and Massachusetts. (J Pediatr 2019;-:1-5)

Predictors of Mortality after Primary Discharge from Hospital in Patients with Esophageal Atresia

Sharman P. Tan Tanny, MBBS, BMedSci, DCH, MSc[1,2,3], Edward Fearon, MD[2,3],
Alisa Hawley, MN, BN, RN, RM, Neonatal Critical Care (Cert)[1,2,4], Jo-Anne Brooks, RN, RM, ENB 408 Neonatal option[1,2,4],

- **Objective:** establish risk factors for mortality in patients with esophageal atresia, focus on risk factors that contribute to death after the primary discharge from hospital.

- **Study design:** retrospective cohort from The Royal Children's Hospital, Melbourne (1980-2018), with esophageal atresia who subsequently died. Mortality before discharge was defined as death during the initial admission.

Table I. Characteristics of the mortality before discharge and mortality after discharge groups

Characteristics	Mortality before discharge (n = 66)	Mortality after discharge (n = 22)	*P* value
Age at death	7 d (0-165 d)	16 mo (3-358 mo)	<.001
Age of mothers, y	31.5 (17-43)	25 (17-37)	.02
Prematurity	65.6% (42/64)	55% (11/20)	.54
Gestational age, wk	34.5 (25-42)	36 (30-40)	.22
Low birth weight	31.3% (20/64)	5.0% (1/20)	.02
Birth weight, g	1895 (660-4100)	2018 (1386-4005)	.08
Male:female	35:31	13:9	.63

Values are median (range) unless otherwise specified.

88/650 patients died (total mortality rate 13.5%)

66/88 (75%) occurred during initial admission (before discharge)

Table II. Numbers of mortality before discharge and mortality after discharge deaths by time period

Groups	1980-1989	1990-1999	2000-2009	2010-2018
Mortality before discharge deaths	22	19	15	10
Mortality after discharge deaths	8	4	4	6
Total patients	153	157	166	174
Mortality rate	19.6%	14.6%	11.4%	9.2%

Mortality rates by time epoch

Table III. Causes of death in the mortality after discharge group (n = 17)

Causes of death	n (%)
Respiratory compromise	6 (35.3)
Aspiration-related complications	
Tracheostomy or airways complications	
Croup	
Sudden deaths	6 (35.3)
Sudden infant death syndrome	
Unexpected death at >1 year old	
Fanconi anaemia-related deaths	2 (11.8)
Trauma	1 (5.9)
Renal failure	1 (5.9)
Plasmacytosis	1 (5.9)

Mortality after discharge 22/580 (3.8%)

Table IV. Distribution of esophageal atresia type within the mortality before discharge and mortality after discharge groups

Esophageal atresias	Mortality before discharge (n = 66)	Mortality after discharge (n = 22)
Type A	7 (10.6)	1 (4.5)
Type B	2 (3.0)	0 (0)
Type C	56 (84.8)	18 (81.8)
Type D	0 (0)	0 (0)
Type E	0 (0)	2 (9.1)
Other variant: Esophagobronchial fistula with tracheal atresia	1 (1.5)	0 (0)
Unrecorded	0 (0)	1 (4.5)

Values are number (%).

Mortality according Gross classification

Predictors of Mortality after Primary Discharge from Hospital in Patients with Esophageal Atresia

Sharman P. Tan Tanny, MBBS, BMedSci, DCH, MSc[1,2,3], Edward Fearon, MD[2,3], Alisa Hawley, MN, BN, RN, RM, Neonatal Critical Care (Cert)[1,2,4], Jo-Anne Brooks, RN, RM, ENB 408 Neonatal option[1,2,4], Assia Comella, BMedSci[1,2,5], John M. Hutson, AO, BS, MD(Monash), MD, DSC(Melb), FRACS, FAAP[1,2,3], Warwick J. Teague, MBBS, DPhil Oxon, FRACS[1,2,3], Anastasia Pellicano, MBBS, FRACP[4], and Sebastian K. King, MBBS, PhD, FRACS[1,2,3,6]

Conclusions:

- Esophageal atresia has an overall survival rate of 83%-95%.
- Overall mortality rate 13.5% (1980s) to 9.2% (2010s).
- Early mortality (initial admission) 75% - Late mortality 25% of all cases of death.
- Mortality after discharge affected 3.8% of patients.
- Leading causes: respiratory compromise, sudden unexplained deaths, and Fanconi anemia.