

Strategy for EA + TOF Repair in Premature

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Introduction

- Esophageal atresia(EA) with Tracheo-esophageal Fistula (TOF) repair is a complex operation, even in full-term neonates
- Successful operative approach is much more likely in the neonate with
 - (1) relative freedom of pulmonary complication,
 - (2) sufficient size to permit a comfortable esophageal anastomosis, and
 - (3) sufficient vigor to withstand a thoracotomy and its postoperative difficulties.

J. Thoracic and Cardiovas. Surg. Vol. 44,September, 1962

Esophageal atresia

- The major factors leading to death in infants with esophageal atresia and tracheoesophageal fistula are
 - (1) pulmonary complications,
 - (2) prematurity,
 - (3) associated major congenital anomalies, and
 - (4) anastomotic leaks with sepsis.

J. Thoracic and Cardiovas. Surg. Vol. 44, September, 1962

Low Birth Weight Neonates

- LBW = 1.5 - 2.5kg
- VLBW = 1.0 - 1.5 kg
- ELBW = < 1.0 kg

- Preterm babies with ELBW/VLBW present with **cardio-pulmonary vulnerability**, an **immature immune system**, and the **risk of preterm complications** such as necrotizing enterocolitis and intracranial hemorrhage (ICH)

In general

- Improvement of survival of EA in LBW babies are due to
 - Improve surgical technique
 - Better understanding of physiology of premature babies
 - Advancement in neonatal intensive care unit
 - Better preoperative preparation, anaesthesia, postoperative care

EA in VLBW neonates

- Management of EA in VLBW neonates remain controversial and continues to be a major surgical challenge
- Specifically those infants with major cardiac anomalies as well as neonates with severe respiratory distress syndrome are less likely to tolerate the surgery and the operative time required for primary repair

Spitz Classification(1994)

Group	Features	Survival (%)
I	>1500 grams , no major cardiac anomaly	98.5
II	< 1500 grams or major cardiac anomaly	82
III	< 1500 grams and major cardiac anomaly	50

Treatment strategies

- Two different treatment strategies for patients with EA and VLBW.
 - The first is primary repair— ligation of the TEF and esophageal anastomosis. The operation time, and anesthesia time are longer. In addition, esophageal tissue is very vulnerable and thin in VLBW, complicating the esophageal anastomosis.
 - The second is staged repair – ligation of the TEF, and gastrostomy is performed to enterally feed the child. Esophageal anastomosis is delayed until the patient stabilizes and gains sufficient weight, usually >1500-2,000 g.

- Some argue that the anastomotic result after primary EA repair is favorable compared with staged repair
- In contrast, others advocate that primary fistula ligation followed by gastrostomy and delayed esophageal anastomosis achieved better outcomes and lowered the rate of anastomotic complications in ELBW infants

TABLE 3 | Literature on esophageal atresia (EA) repair in very low birth weight (VLBW)/extremely low birth weight (ELBW).

Author	Year	Period	n ¹	Weight	Primary	Staged	EA Type	Aim of the study	Conclusion
Schmidt et al. (15)	2017	2002–2016	11	4 ELBW 7 VLBW (24 > 1,500 g)	4	7	Gross C	Compare outcome after primary open repair in VLBW/ELBW with BW > 1,500 g	Complications are unrelated to bodyweight
Hannon et al. (16)	2016	1993–2015	9	ELBW (m ² = 815 g)	2	7	All	Outcome of EA repair in ELBW	56% survival, due to immaturity; Gross A with staged repair, 100% survival
Zani et al. (17)	2016	2000–2014	7	ELBW (m = 930 g)	1	6	All	Outcome of EA repair in ELBW	Complications associated with prematurity
Margain et al. (18)	2014	2012–2013	3	ELBW (m = 690 g)		3	Gross C	Outcome of EA repair in ELBW treated with LEB ³ and delayed repair	LEB enables delayed repair (> 2100g)
Ito et al. (19)	2013		1	ELBW (471 g)		1	Gross C	Case report: Delayed primary repair after EB ⁴	Complications associated with prematurity EA repair was performed too late
Petrosyan et al. (20)	2009	1987–2008	25	VLBW (m = 1380 g)	16	9	All	Comparison between primary and staged repair in EA	Significantly more complications after primary repair
Seitz et al. (21)	2006	2002–2004	4	VLBW (m = 920 g)	4		Gross C	Outcome of EA in VLBW	Primary repair is technically feasible, AI and AS in 25%
Chahine and Ricketts (5)	2000	1981–1999	10	VLBW (m = 1160 g)	1	9	all	Outcome of EA in VLBW	10% died after sepsis caused by AI GER and fundo in 62.5%
Driver et al. (22)	1997		1	ELBW (740 g)	1		Gross C	Case report	Good outcome due to improved NICU treatment
Alexander et al. (23)	1993	1966–1986	21	<2,000 g (1590 g)	4	17	all	Comparison between primary and staged repair in EA	Staged repair incurred a lesser morbidity
Schaarschmidt et al. (24)	1992		1	ELBW (445 g)		1		Delayed primary repair without ligation of TEF ⁵ , Case report	No operation-associated complications
Todd et al. (25)	1990		1	ELBW (700g)		1		Outcome of EA (IIIb) and delayed repair after LEB ³ , Case report	Mechanical ventilation after LEB ³ dilatates the distal esophagus

Overview of the literature regarding the repair of EA with or without TEF in patients born with exclusively ELBW and VLBW, without the claim of completeness.

1 n, number of patients

Outcome of Patients With Esophageal Atresia and Very Low Birth Weight ($\leq 1,500$ g)

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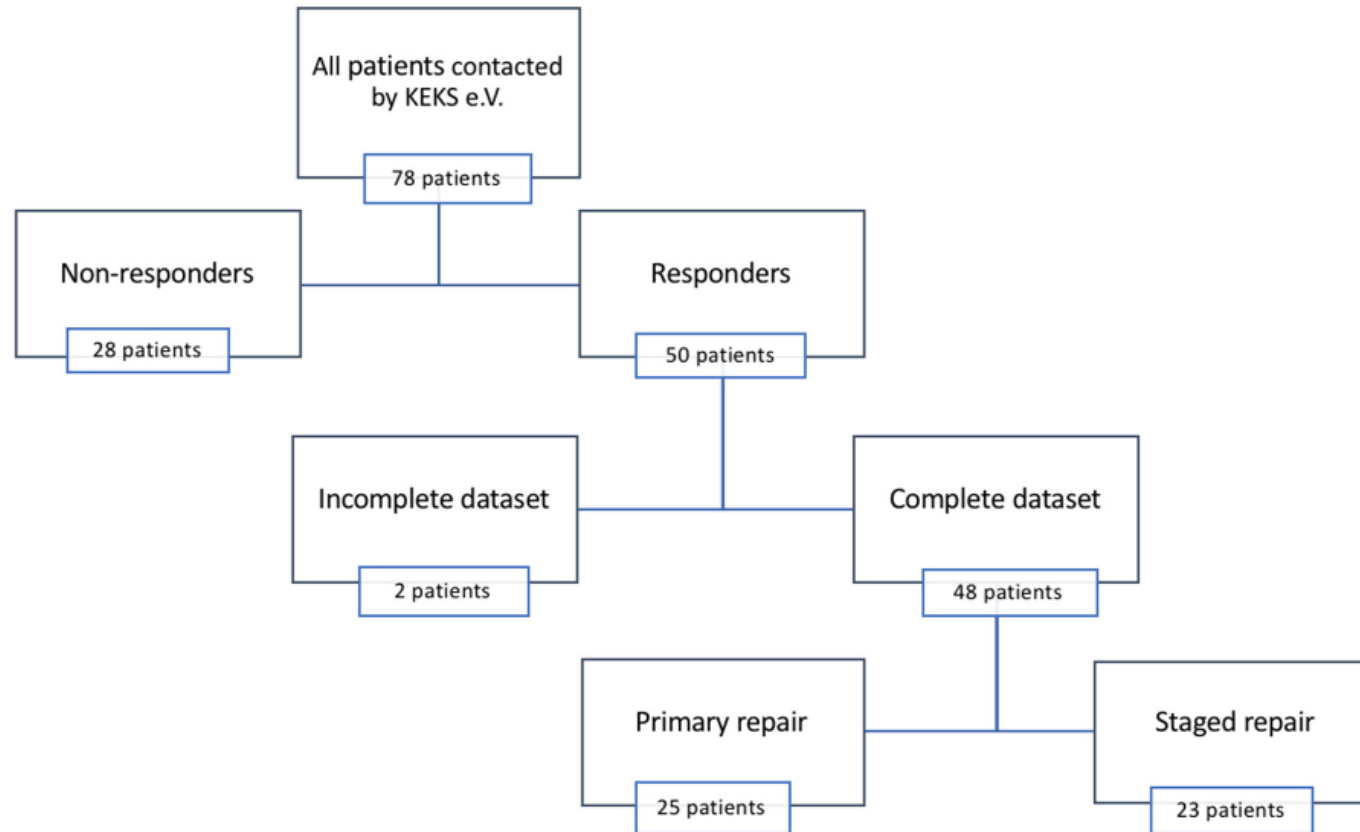


FIGURE 2 | Drop-out analysis.

TABLE 1 | Epidemiological data.

		All	Primary	Staged	P-value*
Male	Yes	21	8 (38%)	13 (62%)	0.09
	No	27	17 (63%)	10 (37%)	
ELWB	Yes	10	4 (40%)	6 (60%)	0.4
	No	38	21 (55%)	17 (45%)	
EA type/Gross	A	7	0 (0%)	7 (100%)	0.01
	B	1	1 (100%)	0 (0%)	
	C	37	21 (67%)	16 (43%)	
	D	2	2 (100%)	0 (0%)	
	Unknown	1	1 (100%)	0 (0%)	
Congenital heart disease	Yes	16	9 (56%)	7 (44%)	0.7
	No	30	15 (50%)	15 (50%)	
	Unknown	2	1 (50%)	1 (50%)	
Heart function	Normal	41	21 (51%)	20 (49%)	0.9
	Affected	5	3 (60%)	2 (40%)	
	Unknown	2	1 (50%)	1 (50%)	
VACTERL association	Yes	11	6 (55%)	5 (45%)	0.9
	No	35	18 (51%)	17 (49%)	
	Unknown	2	1 (50%)	1 (50%)	
Congenital anomalies	Yes	21	12 (57%)	9 (43%)	0.7
	No	25	11 (44%)	14 (56%)	
	Unknown	2	2 (100%)	0 (0%)	
Intracranial haemorrhage	Yes	11	7 (64%)	4 (36%)	0.4
	No	35	17 (49%)	18 (51%)	
	Unknown	2	2 (100%)	0 (0%)	
Preoperative ventilation	Yes	33	17 (52%)	16 (48%)	0.5
	No	11	7 (64%)	4 (36%)	
	Unknown	4	1 (25%)	3 (75%)	
Time to fistula closure	< 24h	11	7 (64%)	4 (36%)	0.8
	>24 h, <48h	9	7 (78%)	2 (22%)	
	>48 h, <5 d	8	4 (50%)	4 (50%)	
	>5 d, <7 d	2	1 (50%)	1 (50%)	
	>7d	8	5 (63%)	3 (37%)	
	No fistula	7	0 (0%)	7 (100%)	
	Unknown	3	1 (33%)	2 (67%)	

TABLE 1 | Continued

		All	Primary	Staged	P-value*
RF	Yes	8	7 (88%)	1 (12%)	0.02
	No	27	12 (44%)	15 (56%)	
	Unknown	13	6 (46%)	7 (54%)	
AS	Yes	24	14 (58%)	10 (42%)	0.5
	No	13	6 (46%)	7 (54%)	
	Unknown	11	5 (45%)	6 (55%)	
Gastrostomy	Yes	28	8 (29%)	20 (71%)	0.01
	No	16	14 (88%)	2 (12%)	
	Unknown	4	3 (75%)	1 (25%)	
GER	Yes	31	13 (42%)	18 (58%)	0.02
	No	12	10 (83%)	2 (17%)	
	Unknown	5	3 (60%)	2 (40%)	

*This table shows all the information collected. Statistical correlation of primary repair and each category (e.g., EA type: A,B, C, D) was tested. *The p-value relates to the category, not the single parameter in a category, and is calculated without unknown cases performing chi-square test. Statistically significant p-values are underlined and marked in bold.*

EELBW, Extremely low birth weight; EA, Esophageal atresia; VACTERL, Vertebral, intestinal atresia, cardiac, tracheal, renal, limb malformations; No., Number; AI, Anastomotic insufficiency; RF, Recurrent fistula; AS, Anastomotic stenosis; GER, Gastroesophageal reflux.

TABLE 2 | Outcome after primary vs. staged repair in the different subgroups.

Subgroup			AI	RF	AS	GER	1 surg.	2 surg.	3 surg.	> 3 surg.	ICH
All patients	All	48 (100%)	9 (19%)	8 (17%)	24 (50%)	31 (65%)	9 (18%)	11 (23%)	4 (8%)	21 (44%)	11 (23%)
	Primary	25 (100%)	6 (24%)	7 (28%)	14 (56%)	13 (52%)	9 (36%)	5 (20%)	2 (8%)	8 (32%)	7 (28%)
	Staged	23 (100%)	3 (13%)	1 (4%)	10 (43%)	18 (78%)	/	6 (26%)	2 (9%)	13 (57%)	4 (17%)
VLBW + ELBW + Type C	All	37 (100%)	6 (16%)	6 (16%)	18 (48%)	21 (57%)	9 (24%)	9 (24%)	3 (8%)	15 (40%)	11 (30%)
	Primary	21 (100%)	5 (24%)	5 (24%)	12 (57%)	5 (48%)	9 (43%)	5 (24%)	1 (5%)	5 (24%)	7 (33%)
	Staged	16 (100%)	1 (6%)	1 (6%)	6 (37%)	11 (69%)	/	4 (25%)	2 (12%)	10 (62%)	4 (25%)
eVLBW	All	38 (100%)	7 (18%)	7 (18%)	17 (45%)	24 (63%)	8 (21%)	8 (21%)	4 (10%)	15 (40%)	5 (13%)
	Primary	21 (100%)	6 (29%)	6 (29%)	10 (48%)	10 (48%)	8 (38%)	4 (19%)	2 (10%)	6 (29%)	4 (19%)
	Staged	17 (100%)	1 (6%)	1 (6%)	7 (41%)	14 (82%)	/	4 (24%)	2 (12%)	9 (53%)	1 (6%)
eVLBW + Type C	All	28 (100%)	5 (18%)	5 (18%)	12 (43%)	15 (54%)	8 (28%)	6 (21%)	3 (11%)	10 (35%)	5 (18%)
	Primary	18 (100%)	5 (28%)	4 (22%)	9 (50%)	8 (44%)	8 (44%)	4 (22%)	1 (6%)	4 (22%)	4 (22%)
	Staged	10 (100%)	0 (0%)	1 (10%)	3 (30%)	7 (70%)	/	2 (20%)	2 (20%)	6 (60%)	1 (10%)
ELBW	All	10 (100%)	2 (20%)	1 (10%)	7 (70%)	7 (70%)	1 (10%)	3 (30%)	0 (0%)	6 (60%)	6 (60%)
	Primary	4 (100%)	0 (0%)	1 (25%)	4 (100%)	3 (75%)	1 (25%)	1 (25%)	0 (0%)	2 (50%)	3 (75%)
	Staged	6 (100%)	2 (33%)	0 (0%)	3 (50%)	4 (67%)	/	2 (33%)	0 (0%)	4 (67%)	3 (50%)
Type A	All	7 (100%)	1 (14%)	/	4 (57%)	7 (100%)	/	2 (29%)	0 (0%)	3 (43%)	0 (0%)

AI, Anastomotic insufficiency; RF, Recurrent fistula; AS, Anastomotic stenosis; GER, Gastroesophageal reflux; Surg., Surgery; ICH, Intracranial hemorrhage; VLBW, Very low birth weight ($\leq 1,500$ g); ELBW: Extremely low birth weight ($\leq 1,000$ g); eVLBW, Exclusively VLBW ($> 1,000$ g; $\leq 1,500$ g).

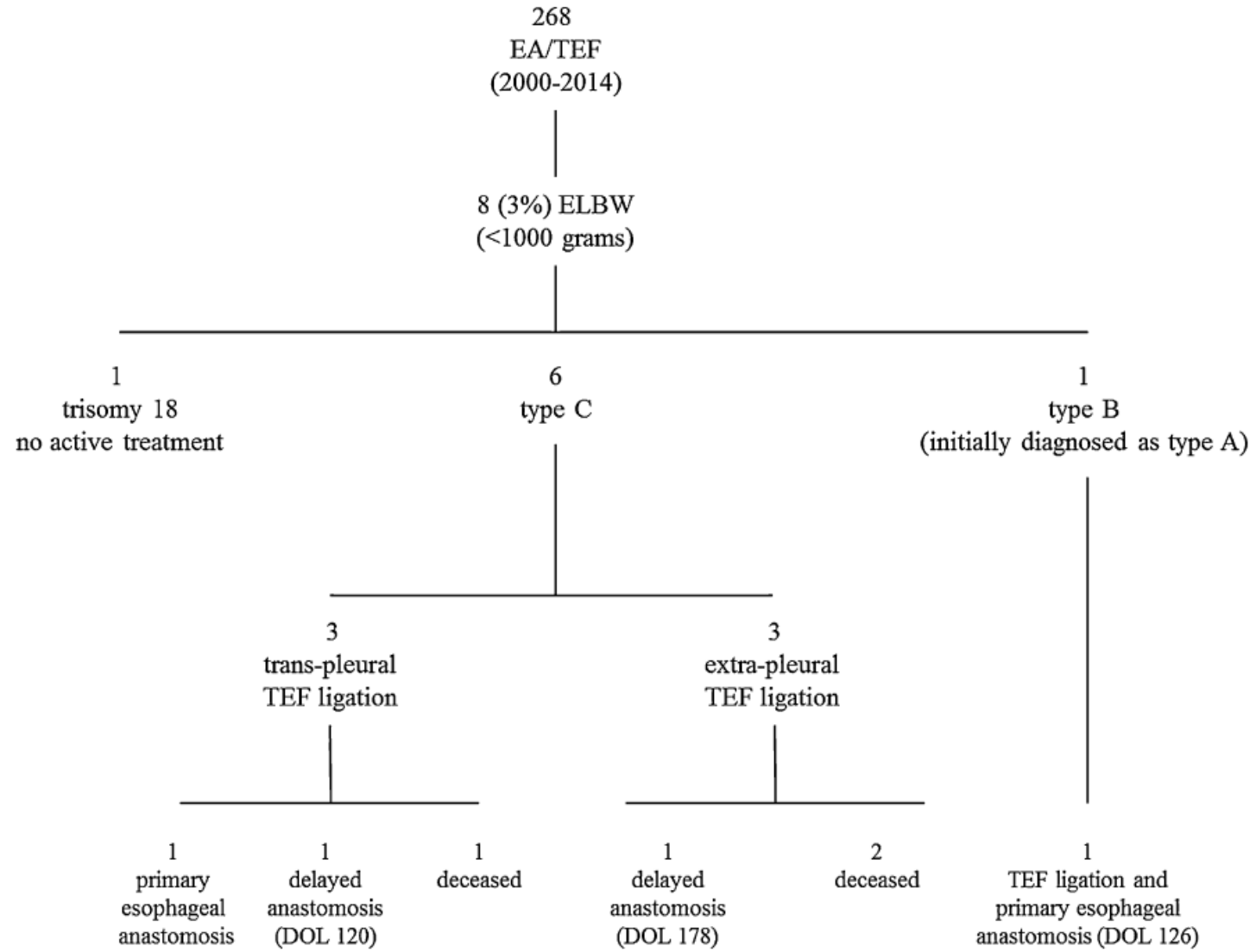
Outcome of esophageal atresia/tracheoesophageal fistula in extremely low birth weight neonates (<1000 grams)

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Table 1 Extreme low birth weight patients with esophageal atresia with/without tracheoesophageal fistula: demographics and description

Gender	Birth weight (g)	Gestational age (weeks)	Antenatal scans	Associated anomalies
1 M	750	26 + 1	Normal	PDA
2 F	980	31 + 3	Polyhydramnios, severe IUGR, 2 vessel cord	VSD, PDA, duodenal atresia, anorectal malformation, omphalomesenteric duct
3 M	995	28 + 4	Normal	Truncus arteriosus
4 F	990	32 + 6	Severe IUGR, single pelvic kidney, single umbilical artery	VSD, PDA, PFO, butterfly vertebra, anorectal malformation, tethered cord, fused pelvic kidney
5 F	870	27 + 1	Oligohydramnios, left talipes, 2 vessel cord, Mosaic uniparental disomy of chromosome 14 (amniocentesis)	Trisomy 14, PDA, PFO, ASD, fused vertebrae, tethered cord, talipes
6 F	975	29 + 5	Bilateral choroid plexus cysts	Trisomy 18
7 F	884	32 + 4	Polyhydramnios, severe IUGR	ASD, tethered cord
8 M	540	23 + 2	Normal, dichorionic diamniotic pregnancy	PDA

ASD atrial septal defect, IUGR = PDA = patent ductus arteriosus, PFO patent foramen ovale, VSD ventricular septal defect



- Overall mortality was 50 %.
- All four surviving patients experienced postoperative complications.
 - One patient had a thoracic duct injury that was successfully treated conservatively.
 - Two (50 %) patients had anastomotic leak that was successfully managed non-operatively with antibiotic and chest tube drainage.
 - Three patients (75 %) developed esophageal strictures requiring balloon dilatation.
 - One patient had severe tracheomalacia requiring aortopexy after esophageal repair

- the incidence of ELBW infants with EA/ TEF is rare (3 %) but these patients have a mortality rate of 50 %.
- The causes of death are mainly due to complications not associated with EA/TEF.
- Early TEF ligation followed by delayed esophageal repair can achieve a good outcome for ELBW infants.
- ELBW neonates with EA/TEF, associated anomalies represent a major risk factor for mortality

ORIGINAL ARTICLE

Review of Oesophageal Atresia and Tracheoesophageal Fistula in Hospital Sultanah Bahiyah, Alor Star, Malaysia from January 2000 to December 2009

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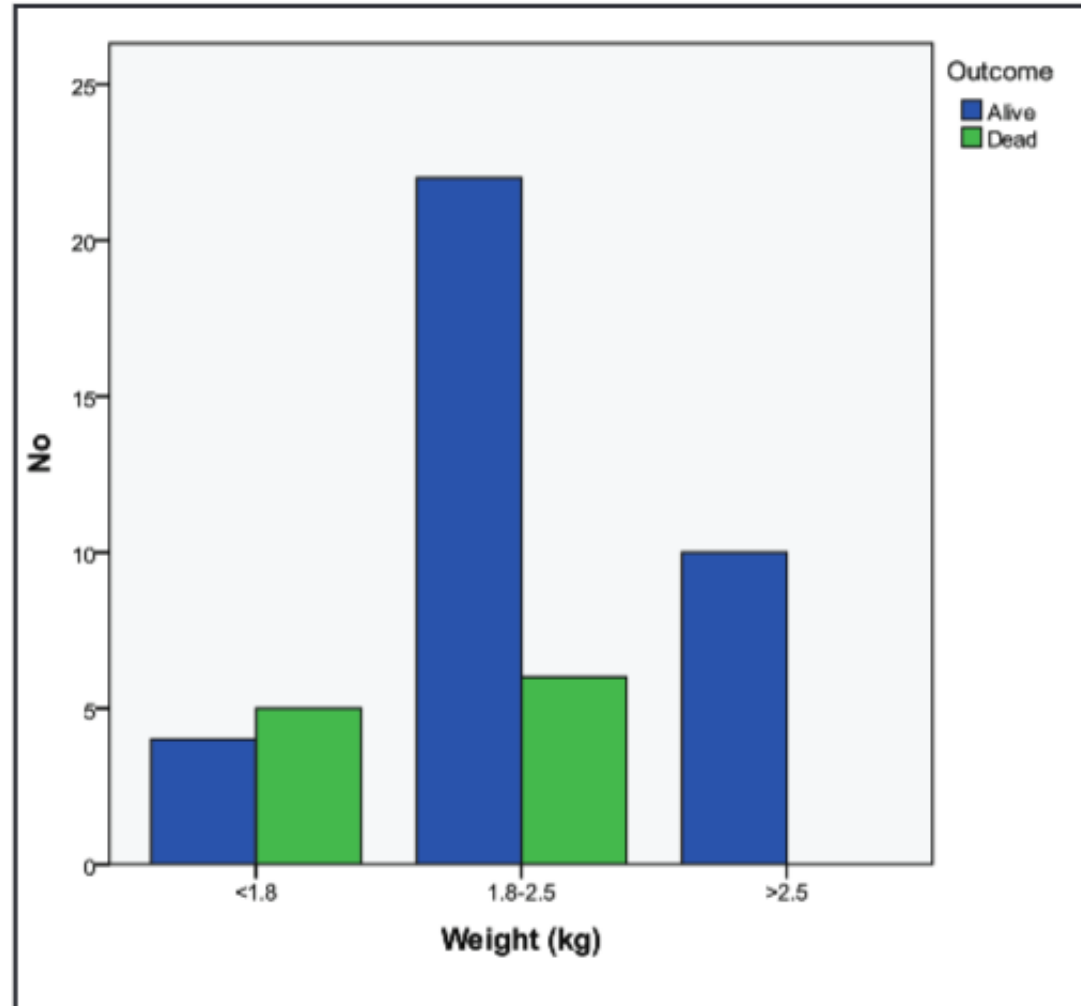


Fig. 2: Comparison of birth weight and outcome of EA/TEF patients in HSB from Jan 2000 to Dec 2009.



YEAR	OA + TOF 2005 - 2010						primary re staged repair	mortality	comorbid
	total	prem 30 -	prem < 30	wt 2.1 - 2.	wt 1.5 - 2.	wt 1.0 - 1.			
2005	14	34			1.8		primary repair		
		33				1.54	primary repair		
		33			1.75		primary repair		
		35		2.2			primary repair	Single ventricle, PDA	
		term		2.4			primary repair	cardiac tof	
		term		2.45			primary repair	Leak-conservative	
2006	23		26			0.625	primary repair	died - chronic lung, IVH3, ?Leak	
		33				1.38	primary repair		
		36		2.1			primary repair	died - cvl sepsis, coarc aorta	
		33				1.45	primary repair	died - chro ARM	
		34				1.34	primary repair		
						1.92	primary repair		
		term				1.93	primary repair	ARM	
		37		2.41			primary repair	tracheal stenosis	
		term				2.05	primary repair	Died at ho Cardiac ToF	
		term		2.2			primary repair		
		38		2.18			primary repair	Leak- redo repair	
2007	15		27			1.05	primary repair	died - chronic lung	
			29			1.22	staged repair		
			29			1	staged repair		
		38		2.15			primary repair		
		term		2.16			primary repair		
2008	26	34				1.2	staged rep delayed 1 repair pod7		
		32				1.2	primary repair		
		30				1.3	staged rep delayed 1 repair pod30		
		32				1.3	primary repair		
		31				1.48	staged repair	died - NEC, Down synd, Cardiac TOF	
		30				1.7	primary repair		
		term				1.45	primary repair		
		term		2.1			primary repair		
		term				1.94	primary repair		
2009	23	35				1.26	primary repair		
		36				1.47	primary repair	died - dysmorphic, PRS	
		33				1.6	staged repair	died	
		36		2.19			primary repair	died - Edward	
		36				1.7	primary repair	died - recurrent fistula	
		30				1.46	staged rep delayed 1	died - aspirated	
		35				1.93	primary repair	cervical myotomy	
		35		2.37			primary repair		
		36				1.85	primary repair		
		term				1.9	primary repair		
2010	22								
		32				1.45		died - Down, Cardiac TOF, hypercyanotic spell. No op done	
		34				1.29	staged repair	esophagostomy	
		36		2.06			primary repair	died - sepsis, duod atresia, asp pneum	
		term		2.4			primary repair		

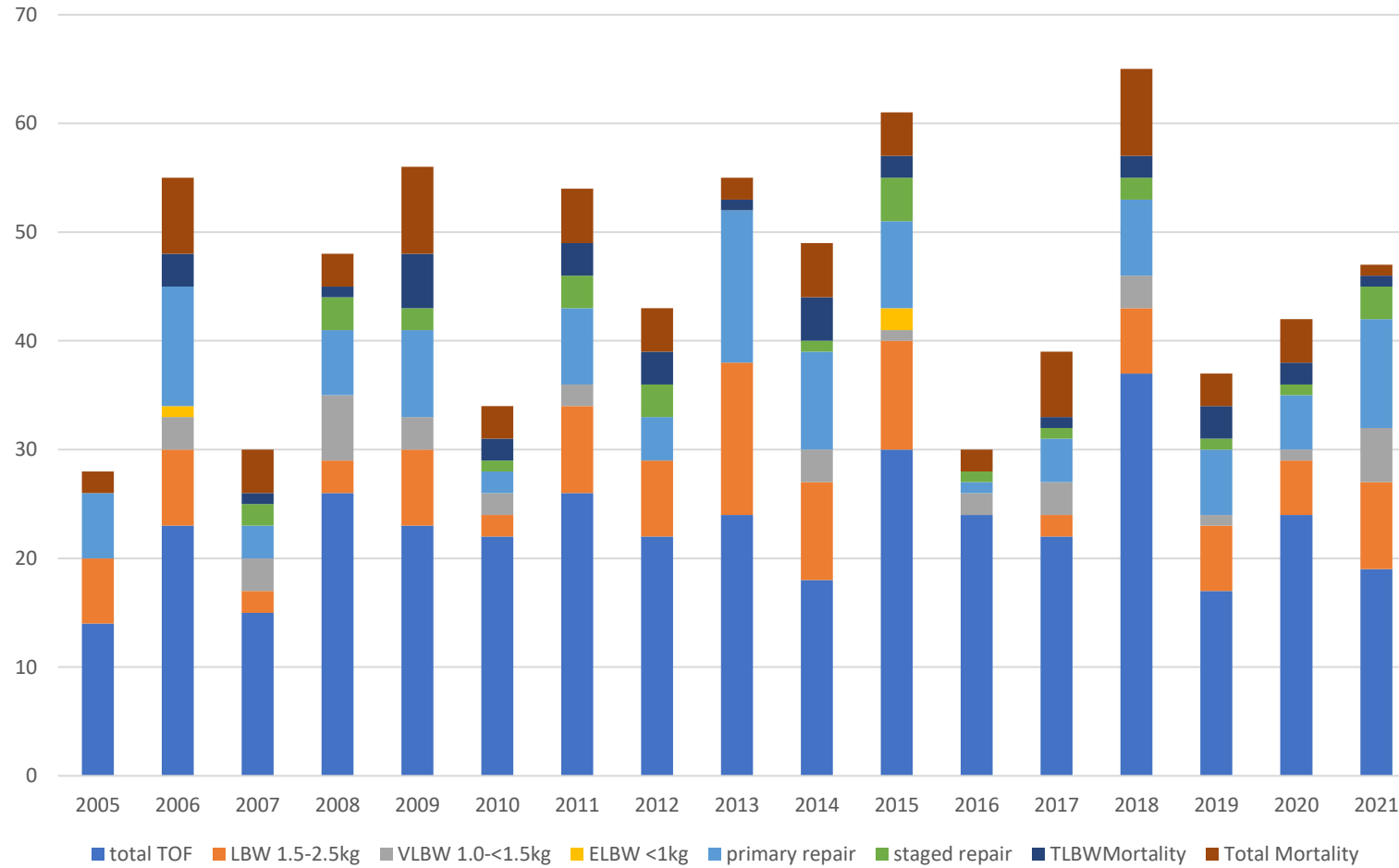
YEAR	total	OA + TOF 2011 - 2015				primary re staged repair	mortality
		prem 30 -	prem < 30 wt 2.1 - 2.	wt 1.5 - 2.	wt 1.0 - 1.		
2011	26						
		35	2.1		primary repair	ARM, Duod atresia	
		32		1.2	primary repair		
		35	2.35		primary repair		
		34	1.73		primary repair	Leak, converted to pure atresia, gastrostomy	
		33	1.5		staged rep delayed repair pod4	desat intraop, later noted Trisomy18	
		34	1.5		primary repair	stricture - dilate	
		34	1.7		staged rep delayed repair pod3		
		32		1.05	staged repair	died - lung problem	
		34	1.9		primary repair	died - sepsis	
		term	1.9		primary repair	died - pphr redo op pod3	
2012	22						
		35	1.92		staged repair	died - mult DA, ARM, Uret hypop	
		35	1.9		staged repair	severe cardiac - single atrium, ventricle	
		36	1.56		primary repair	cardiac tof	
		33	1.07		primary repair		
		term	2.12		primary repair	died - asp pneu	
		term	2.08		primary repair	died - seps ARM, DA	
		35	2.05		staged repair	Tof type B, esophagostomy	
2013	24						
		36	2.23		primary repair	ARM-anoplasty	
		36	2		primary repair		
		35	1.91		primary repair		
		36	1.6		primary repair	Leak- conserv	
		36	2.09		primary repair	DA, ARM	
		34	1.84		primary repair		
		35	2.1		primary repair	stricture-dilate	
		32	1.62		primary repair		
		34	1.85		primary repair	Cardiac tof, ARM	
		36	1.95		primary repair	DA	
		36	1.77		primary repair	died -complex heart	
		term	2.09		primary repair		
		term	1.64		primary repair	Leak-conserv, PDA in failure	
		term	2.2		primary repair	leak-conserv	
2014	18						
		term	2.42			died in ot post-bronch desat, cpr 1 hr, no murmur	
		term	2.3		primary repair		
		term	1.57		primary repair	tof repair with lap for gastric perf	
		36	1.75		primary repair	hypoplastic Lt lung,	
		term	2.2		primary repair		
		34	1.75		primary repair		
		34		1.4	primary repair	died - sepsis, MOF	
		36	1.63		primary repair		
		term	2.45		primary repair		
		34		1.45	primary repair	died 1st op in sjmc, leak, PDA in failure	
		34	1.8			died - No op, cardiac tof, bronc stenosis, absent RLL & LLL	
		33		1.1	staged repair		
2015	30						
		31		0.9	primary repair	Leak, converted to pure OA	
		31	1.9		primary repair	stricture-dilate	
		36	2.1		primary repair	dysmotility, tracheomalacia, Aortopexy done	
		30		1.15	staged rep delayed repair after 2 mth		
		27		0.94	staged repair	died-resp f 1st fistula ligation done in Kajang, refistula	
		term	2.06		primary repair		
		36	1.7		primary repair	VSD in failure	
		34	1.5		primary repair	ARM	
		term	2.25		staged rep delayed repair pod3	hypoplastic Lt heart	
		36	2.35		primary repair	LPA stenosis	
		term	1.94		staged repair	pu atresia, large vsd	
		term	2.42		primary repair	DA	
		term	1.63			died at home - discharged home, Edward syndrome	

YEAR	total	OA + TOF 2016 - 2021				primary re staged repair	mortality
		prem 30 - 34	prem < 30	wt 2.1 - 2.0	wt 1.5 - 2.0		
2016	24	34				primary repair	ARM
		34				Staged repair	tracheal tear, esophagostomy, recurrent fistula
2017	22	33				primary repair	
		32				primary repair	leak - conservative
			29			staged rep delayed repair pod4	stricture - dilatation
		36				primary repair	
		35				primary repair	died - complex heart
2018	37	34				primary repair	
		33				primary repair	died
		33				primary repair	
		31				staged repair	TOF type D
		32				staged repair	died - com ARM, Absent pulm artery
		34				primary repair	ARM
		31				primary repair	stricture, dilatation
		36	2.15			primary repair	ARM - Anoplasty
		34				primary repair	stricture, dilatation
2019	17	36				primary repair	died - perf leak, converted to pure OA, Cardiac ToF
		33				primary repair	cyanotic heart on prostin
		36				primary repair	leak, reanastomosed
		36				primary repair	ARM, stricture- dilate
		34				primary repair	
						staged repair	died - bil. L esophagostomy pod3
						primary repair	died - Rt lung hypoplasia
2020	24	34				primary repair	duod atresia
		32	2			primary repair	died -MOF
		32				primary repair	stricture - dilate, coarc aorta
			2.03			primary repair	
			2			primary repair -Kuantan	leak, refistula,esophagostomy
		33				staged repair	died aortic injury
2021	19	34				primary repair	stricture- dilate
		32				primary repair	dysmorphic
		34				primary repair	ARM, stricture- dilate
						staged repair	died- cardiac tof, infundibular spasm
						primary repair	severe tracheomalacia
						primary repair	ARM
		33				primary repair	
						primary repair	
						staged repair	
		35	2.1			primary repair	severe tracheomalacia
		33				primary repair	stricture - dilate
		36	2.5			staged repair	RUL agenesis, esophagostomy
		36	2.42			primary repair	VSD

YEAR	total TOFLBW 1.5-2.5kg	/LBW 1.0-<1.5kg	ELBW <1kg	primary repair	staged repair	3WMortality	total Mortality	
2005	14	6		6		0	2	
2006	23	7	3	1	11	3	7	
2007	15	2	3		3	2	1	4
2008	26	3	6		6	3	1	3
2009	23	7	3		8	2	5	8
2010	22	2	2		2	1	2	3
2011	26	8	2		7	3	3	5
2012	22	7			4	3	3	4
2013	24	14			14		1	2
2014	18	9	3		9	1	4	5
2015	30	10	1	2	8	4	2	4
2016	24		2		1	1	0	2
2017	22	2	3		4	1	1	6
2018	37	6	3		7	2	2	8
2019	17	6	1		6	1	3	3
2020	24	5	1		5	1	2	4
2021	19	8	5		10	3	1	1
TOTAL	386	102	38	3	111	28	34	71

TLBW % = 143/386 = 37%			
Total Mortality = 71/386 = 18%	TLBW=Total Low Birth Weight		
TLBWMortality = 34/71 = 47%			
TLBWMortality Rate = 34/143 = 23%			

EA + TOF in LBW, VLBW & ELBW in HKL/HTA from 2005 - 2021



Conclusions

- Management of EA + TOF in LBW, VLBW and ELBW neonates are very challenging
- Primary repair for stable neonates
- staged repair for “unstable” neonates and for ELBW neonates
- Esophagostomy for neonates with respiratory compromised

Thank you for your attention