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Neurogenetics disease : issue on ECMO decision

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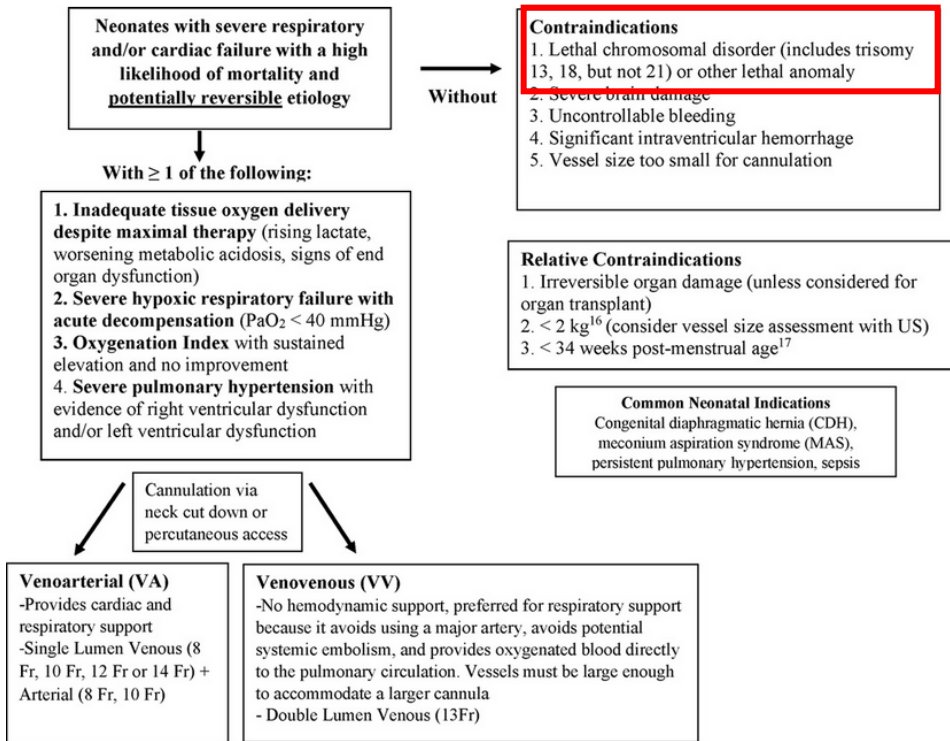
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No Conflict of interest to declare

Introduction

- It is not possible to speak about « genetics disease » or « genetics condition »
- Several pathologies
 - Down syndrom (most frequent genetic disease, 50% of congenital cardiac disease)
 - Trisomy 13, 18
 - CHARGE
 - 22q11 deletion
 - Others ...
- Wide spectrum of neurological impairment
- Wide spectrum of survival rate
- Only few reports on genetics disease except for Down syndrom

ELSO Statement



B. Contraindications

Most contraindications are relative, balancing the risks of the procedure (including the risk of using valuable resources which could be used for others) vs. the potential benefits. The relative contraindications are: 1) conditions incompatible with normal life if the patient recovers; 2) preexisting conditions which affect the quality of life (CNS status, end stage malignancy, risk of systemic bleeding with anticoagulation); 3) age and size of patient; 4) futility: patients who are too sick, have been on conventional therapy too long, or have a fatal diagnosis. See patient-specific protocols for details.

- International survey on patient selection for ECMO
- Cross sectionnal study based on survey
- Main objectif : explore patient selection process

- T13: 91% will never offer ECMO
- T18: 90% will never offer ECMO
- T21 : 3 % will never offer ECMO
- IVH III/IV: 73 % will never offer ECMO
- Post anoxic encéphalopathy : 48 % will never offer ECMO

Table 1 General neonatal ECMO criteria

Gestational age ≥ 34 weeks or birth weight ≥ 2000 g
 No significant coagulopathy or uncontrolled bleeding
 No major intracranial hemorrhage
 Reversible lung disease with length of mechanical ventilation <10–14 days
 No uncorrectable congenital heart disease
 No lethal congenital anomalies
 No evidence of irreversible brain damage

Modified with permission from Van Meurs *et al.*³

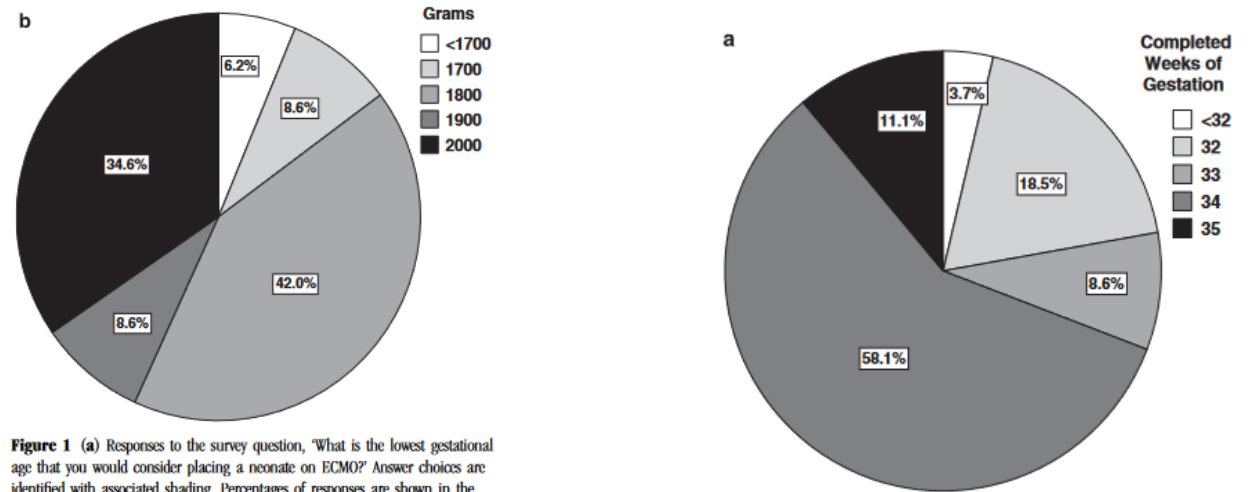


Figure 1 (a) Responses to the survey question, "What is the lowest gestational age that you would consider placing a neonate on ECMO? Answer choices are identified with associated shading. Percentages of responses are shown in the pie chart. (b) Responses to the survey question, "What is the lowest birth weight, assuming that the patient meets your minimum gestational age requirements, that you would consider placing a neonate on ECMO? Answer choices are identified with associated shading. Percentages of responses are shown in the pie chart.

Chapman et al, Journal of perinatology, 2009

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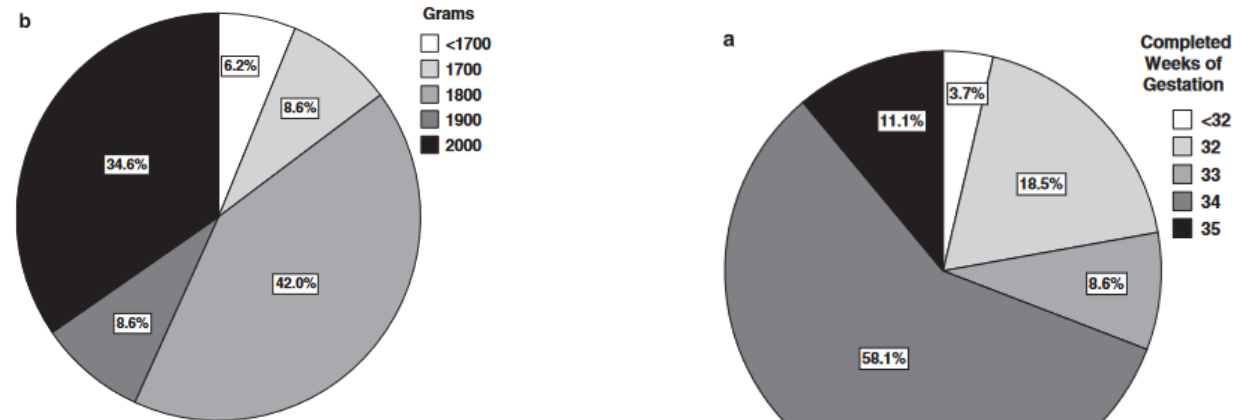


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Pediatric data

- Retrospective ELSO database study, 30 years study period
- 46239 patients on ECMO without T21 and 623 patients on ECMO with T21
- 21 patients every years reported in ELSO database
- Prevalence of T21 receiving ECMO : 13,5/1000

Table I. Characteristics of pediatric patients with T21 before ECMO (n = 623)

Characteristics	Survived (n = 352)	Died (n = 271)	P value
Era, n (%)			.11
1 (1983-1992)	32 (9)	14 (5)	
2 (1993-2002)	108 (31)	97 (36)	
3 (2003-2013)	212 (60)	160 (59)	
Nonwhite race	137 (39)	97 (36)	.96
Weight, kg, median (IQR)	4.0 (3.2-6.0)	4.0 (3.2-5.8)	.88
Age group, n (%)			.005
Neonate (\leq 30 d)	168 (48)	99 (37)	
Child (31 d-18 y)	184 (52)	172 (63)	
Female sex, n (%)	163 (46)	141 (52)	.14
VA ECMO, n (%)	271 (77)	241 (89)	<.001
Cardiac indication for ECMO, n (%)	136 (39)	164 (61)	<.001
Milrinone use, n (%)	32 (9)	53 (20)	<.001
pH <7.24, n (%)	89 (25)	86 (32)	.05
CHD, n (%)	191 (54)	182 (67)	.001
HFOV, n (%)	126 (36)	79 (29)	.04
Nitric oxide, n (%)	175 (50)	103 (38)	.001

HFOV, high-frequency oscillating ventilation.
Values in bold are $P < .05$.

- Research for risk factors associated with T21

Table II. Risk factors for mortality developing after ECMO cannulation in patients with T21 (n = 623)

Factors	Survived (n = 352), n (%)	Died (n = 271), n (%)	P value
ECMO duration >7 d	175 (50)	167 (62)	.003
Complications			
Mechanical	86 (24)	86 (32)	.04
Hemorrhagic	82 (23)	103 (38)	<.001
Surgical site bleed	30 (9)	38 (14)	.017
DIC	3 (1)	9 (3)	.02
Neurologic	29 (8)	58 (21)	<.001
Seizures, clinical	13 (4)	17 (6)	.11
EEG-determined seizure	4 (1)	5 (2)	.46
Intracranial hemorrhage	8 (2)	16 (6)	.02
Ischemic infarct	10 (3)	12 (4)	.25
Renal	72 (20)	130 (48)	<.001
Urine creatinine >1.5 mg/dL	14 (4)	33 (12)	<.001
Hemofiltration required	51 (14)	68 (25)	.008
CWHD required	5 (1)	15 (6)	.004
Dialysis required	4 (1)	13 (5)	.005
Cardiovascular	173 (49)	173 (64)	.003
Pulmonary	16 (5)	29 (11)	.003
Metabolic	56 (16)	71 (26)	.002
Hyperbilirubinemia	10 (3)	24 (9)	.001
Serum glucose >240 mg/dL	23 (7)	31 (11)	.03
Infection	27 (8)	33 (12)	.06

CWHD, continuous veno-venous hemodialysis; DIC, disseminated intravascular coagulation; EEG, electroencephalography.

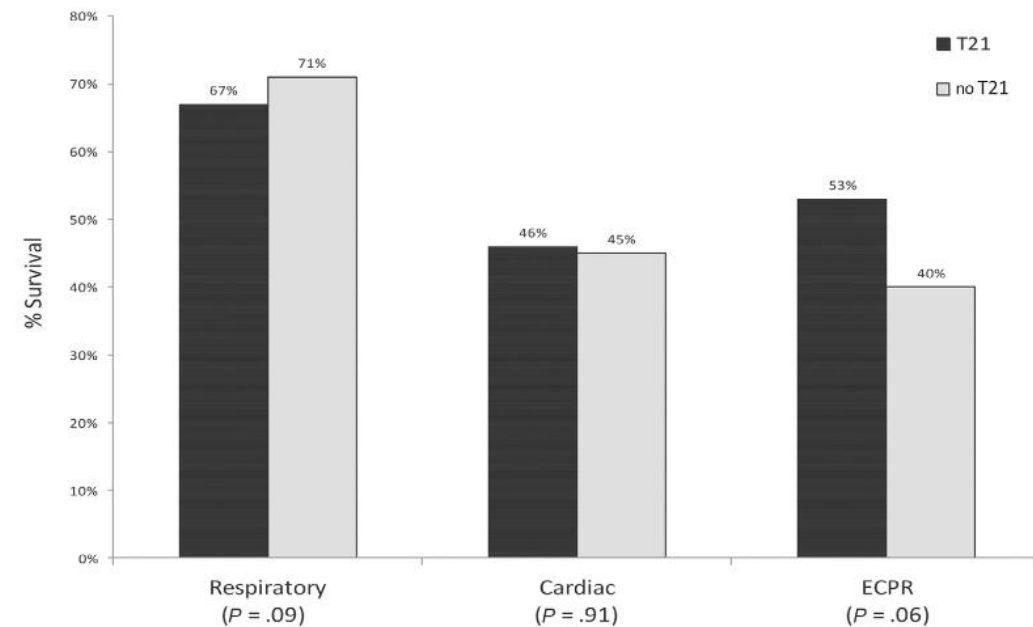


Figure 2. Percent survival to hospital discharge by indication for ECMO in pediatric patients with T21 (n = 623) and those without T21 (n = 46 293). ECPR, extracorporeal cardiopulmonary resuscitation.

- Electronic cross-sectional study, ECMO centers World wide
- Five cases were proposed

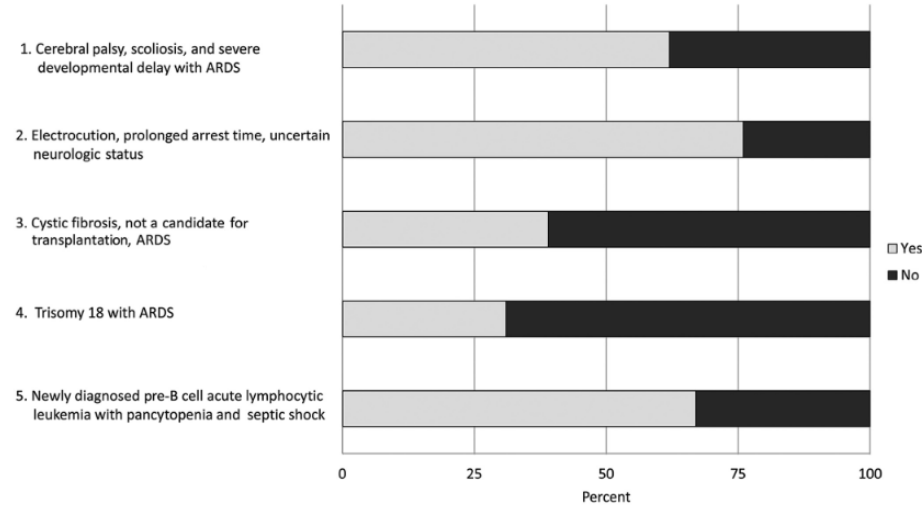


Figure 1. Respondents (%) who would or would not offer ECMO. ARDS, acute respiratory distress syndrome.

	Would you offer ECMO?	
	Yes	No
Cerebral palsy	Quality of life (n = 45) "Although delayed, Her quality of life is good, she communicates and attends school and enjoys it."	"...her severe developmental delay" "Anticipated quality of life post ECMO run"
Postcardiac arrest	Uncertain neurologic outcome (n = 28) "The most important factor in my decision is the uncertain prognosis for the acute injury. So I prefer to buy time with ECMO to properly assess the patient's response."	"Uncertain neurologic status after OHCA at beginning of ECMO is in our institution, a contraindication."
Cystic fibrosis	Transplant status (n = 31) "If he is not a transplant candidate, ECMO is his last chance right now for a few more years."	"Most important factor is that he has a progressive and irreversible condition that is not amenable to transplant."
Trisomy 18	Baseline health status (n = 38) "He has developmental delay but no other significant organ dysfunction."	"He would not even have had cardiac surgery because of trisomy 18; certainly no ECMO."
Pre-B ALL with septic shock	Prognosis (n = 38) "She can recover from her leukemia. I would not let her die from septic shock without trying ECMO."	"Presence of cancer of any type is a poor prognostic indicator for survival with ECMO."

ALL, acute lymphocytic leukemia.

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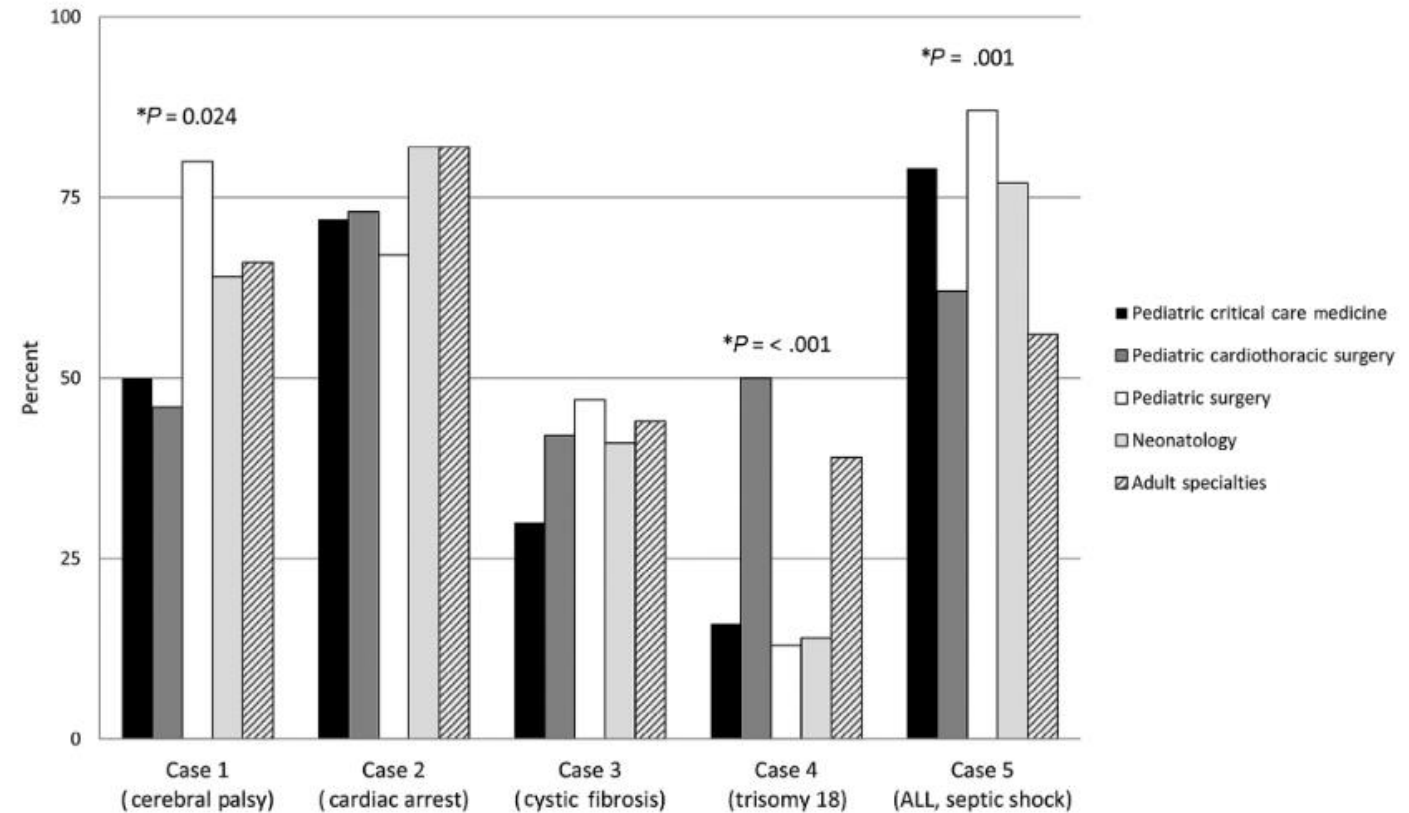


Figure 2. Respondents who would offer ECMO (%) by specialty. ALL, acute lymphoblastic leukemia.

Down syndrome and cardiac surgery

- ELSO database study, 1998 – 2011
- Cardiac surgery for Down syndrome and contrôle group
- Five heart defects: common atrioventricular canal, tetralogy of Fallot, truncus arteriosus, transposition of great vessels

	Total (n = 2,815)	Controls (n = 2,694)	Down syndrome (n = 121)	p value
Age (days)	45 (9–192)	41 (9–189)	133 (59–231)	<0.001
Male: % (n)	55 (1,536)	55 (1,472)	53 (64)	0.71
Weight (kg)	3.8 (3.0–6.1)	3.7 (3.0–6.1)	4.7 (3.6–6.2)	<0.001
Gestation age (weeks)	38.0 (37.0–39.0)	38.0 (37.0–39.0)	38.0 (36.0–38.0)	0.02
Time between admission and ECMO initiation (h)	83.5 (23.0–225.0)	85.0 (23.0–228.0)	42.0 (16.0–174.5)	0.01
Time between intubation and ECMO initiation (h)	24.0 (9.0–101.0)	24.0 (9.0–102.0)	21.5 (9.0–65.8)	0.55
Cardiac arrest before initiation of ECMO: % (n)	35 (993)	35 (946)	39 (47)	0.40
Type of cardiac defect: % (n)				
Transposition of great vessels: % (n)	44 (1,230)	46 (1,226)	3 (4)	<0.001
Tetralogy of Fallot: % (n)	30 (835)	29 (787)	40 (48)	0.01
Common AV canal: % (n)	17 (473)	15 (397)	63 (76)	<0.001
Interrupted aortic arch: % (n)	10 (274)	10 (269)	4 (5)	0.03
Truncus arteriosus: % (n)	9 (249)	9 (247)	2 (2)	<0.001
Reason for ECMO: % (n)				
Respiratory failure	10 (276)	10 (259)	14 (17)	0.11
Cardiac failure	74 (2,090)	74 (2,004)	71 (86)	0.42
ECPR	16 (449)	16 (431)	15 (18)	0.74
Bridge to heart transplant	2 (56)	2 (56)	0 (0)	0.11
Type of ventilator				0.64
Conventional mechanical ventilator	85 (2,386)	85 (2,284)	84 (102)	
High-frequency oscillator ventilation	1 (36)	1 (33)	2 (3)	
Unknown	14 (388)	14 (372)	13 (16)	

	Total (n = 2,815)	Controls (n = 2,694)	Down syndrome (n = 121)	p value
Mortality: % (n)	55 (1,559)	56 (1,506)	44 (53)	0.01
ECMO duration (h)	111.0 (63.0–186.0)	111.0 (63.0–187.0)	118.0 (64.0–178.0)	0.97
Time between ECMO termination and extubation (h)	193.0 (75.0–431.0)	192.0 (71.0–429.0)	260.0 (122.0–504.0)	0.07
Time between ECMO termination and death (h)	4.0 (0.0–266.0)	3.0 (0.0–254.0)	25.0 (0.0–460.0)	0.22
Hospital stay (days)	26.4 (12.6–51.0)	26.2 (12.6–50.2)	29.0 (14.7–54.3)	0.26

- Retrospective cohort study based on pediatric health system information
- Aim : characterizing trends and outcomes in cardiac surgery for patients with genetic condition : T21, 22q11 deletion and other GC
- Large data base ++
- T21 patients have the best outcomes among Genetic conditions

Variable	No known Genetic Condition N=80540	Trisomy 21 N=9473	Trisomy 13/18 N=156	22 q11 N=715	Other Genetic Conditions N=4369
In Hospital Death (n, %)	2344 (3)	194 (2) ^a	20 (13) ^a	33 (5) ^a	274 (6)

Continuous variables summarized by Median and Interquartile Range: 50th (25th-75th).

Categorical variables summarized by % (n).

^aStatistically significant difference between every group compared to no GC, p<.008

^bStatistically significant difference between T21 and 22q11, compared to no GC, p<.008

* Statistically significant difference compared to no GC, p<.008.

Conclusion

- Down syndrom is not a contra-indication to ECMO anymore
- Others genetics disease need to be evaluated with a multidisciplinary meeting
 - Assess the global prognosis (T13 or 22q11 deletion)
 - Assess the prognosis of the acute event
- Wide range of « habits » depending on country, unit, jobs (surgeon, intensivist, neonatologist)
- The presence of most genetic disease have increase mortality with cardiac surgery (except T21)