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Nakata index above 1500 mm^2/m^2 predicts death in absent pulmonary valve syndrome

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Key question

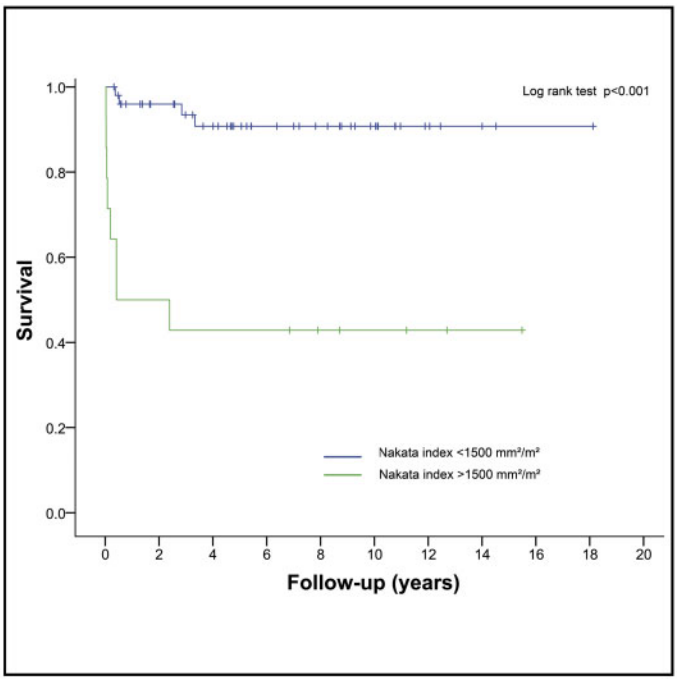
What are the risk factors and cut-off pulmonary artery (PA) size that predict death and prolonged ventilation in absent pulmonary valve syndrome?

Key finding(s)

The Nakata index is a risk factor for mortality; lower weight is a risk factor for prolonged ventilation. The cut-off Nakata index is 1500 mm^2/m^2.

Take-home message

The Nakata index is a risk factor for death in absent pulmonary valve syndrome, with a critical value of 1500 mm^2/m^2, even after PA repair.



Abstract

OBJECTIVES: Absent pulmonary valve syndrome is a rare congenital heart disease with severe airway compression due to dilatation of the pulmonary arteries (PAs). We investigated risk factors for death and prolonged mechanical ventilation (>7 days) and a threshold PA size for these outcomes.

METHODS: This retrospective 2-centre cohort study included 68 patients with complete repair between January 1996 and December 2015.

RESULTS: Median age at repair was 3.9 months (1.3–8.7 months), and median weight was 5 kg (4–7 kg). The mortality rate before hospital discharge was 12%, and the mortality rate at last follow-up was 19%. In multivariable analysis, risk factors for death were higher Nakata index [hazard ratio (HR) 1.001, 95% confidence interval (CI) 1.001–1.002; $P < 0.001$] and lower SpO_2 (HR 1.06, 95% CI 1.02–1.09; $P = 0.002$).

The accuracy of the Nakata index to predict death was excellent (area under the curve at 6 months: 0.92; $P = 0.010$). A Nakata index above 1500 mm^2/m^2 predicted mortality at 6 months with a sensitivity of 98% and a specificity of 82%. Twenty-five patients (37%) had prolonged mechanical ventilation. The only multivariable risk factor for prolonged ventilation was lower weight at repair (odds ratio 2.9, 95% CI 1.3–6.7; $P = 0.008$). Neither PA plasty nor the LeCompte manoeuvre had a protective effect on mortality or prolonged ventilation. A Nakata index above 1500 mm^2/m^2 remained a risk factor for mortality ($P = 0.022$) in patients who had a PA plasty or the LeCompte manoeuvre.

CONCLUSIONS: In patients with absent pulmonary valve syndrome, the Nakata index predicts mortality with a cut-off of 1500 mm^2/m^2. Lower weight at repair is the only multivariable risk factor for prolonged ventilation. Neither PA plasty nor the LeCompte manoeuvre had a protective effect on these outcomes.

Keywords: Absent pulmonary valve syndrome • Mortality • Prolonged mechanical ventilation • Airway management • Nakata index

INTRODUCTION

Absent pulmonary valve syndrome (APVS) is a rare congenital heart disease (CHD) characterized by the absence or dysplasia of pulmonary valve leaflets leading to severe pulmonary regurgitation [1]. It is generally associated with ventricular septal defect in the outlet septum, over-riding aorta and right ventricular outflow tract stenosis [2]. The 22q11 microdeletion (DiGeorge syndrome) is found in 25% of patients with APVS [3]. The main characteristic of APVS is massive dilatation of the pulmonary arteries (PAs), causing severe respiratory symptoms because of tracheal and bronchial compression.

The clinical presentation of APVS depends on the severity of the respiratory symptoms: high morbidity and mortality occur in neonates who present with respiratory symptoms shortly after birth and require prolonged mechanical ventilation (PMV) even after urgent repair, whereas infants and children with mild symptoms are often eligible for elective repair. Survival has improved up to 80% thanks to advances in prenatal diagnosis and surgical and intensive care techniques [4]. Major risk factors for mortality in heterogeneous published surgical series were preoperative ventilation and need for repair in the neonatal period but not PA size [5–7]. No threshold is available in the literature to predict the effect of PA size on airway compression and negative outcomes such as mortality and prolonged ventilation.

The aims of our study were (i) to report clinical and surgical outcome of patients with APVS in 2 French paediatric cardiac surgery centres, with particular attention to respiratory management; (ii) to investigate predictors of mortality and prolonged postoperative ventilation and to find a threshold PA size predicting negative outcomes; and (iii) to evaluate the influence of airway relief by PA plasty and/or the LeCompte manoeuvre.

PATIENTS AND METHODS

Our institutional review board and the local ethics committee approved the retrospective data review, declared to the Commission Nationale Informatique et Libertés (declaration 1923641).

Patient selection

From January 1996 to December 2015, 98 patients presenting with APVS and ventricular septal defect who had first had a complete repair in the Hôpital Marie Lannelongue and in the Hôpital Universitaire Necker-Enfants malades were reviewed. Thirty patients were excluded: 11 had an intact ventricular septum, and 19 came from abroad through humanitarian missions with missing follow-up information.

Preoperative and perioperative variables

Preoperative and perioperative variables were collected (Supplementary Material, Table S1). The population was divided into 3 groups: neonates were <28 days old at repair; infants were between 28 days and 1 year old; and children were more than 1 year old. Preoperative airway compression was evaluated with chest radiographs, or when available, with computed tomographic (CT) scans or bronchoscopy, with details on its localization and its severity described according to published guidelines ([8] for CT scans, [9] for bronchoscopy). Obstruction of the airway lumen below 50% was considered grade I or mild; 50–70% obstruction was grade II or moderate; and >70% obstruction was grade III or severe. All available transthoracic echocardiographic reports before repair were reviewed. PA size was evaluated by echocardiography or thoracic CT scans when available. Using echocardiography, the sizes of the left and right PAs in mm were obtained from the parasternal short-axis view just before the lobar branching as recommended in the guidelines [10]. The Nakata index was calculated as described previously [11], i.e. PA index = sum of cross-sectional area of left and right PAs in mm^2 divided by total body surface area.

Surgical technique

Repair included closure of the ventricular septal defect, enlargement of the right ventricular outflow tract and establishment of right ventricle to PA continuity. Mean cardiopulmonary bypass time was 135 ± 68 min, and the mean aortic cross-clamp time was 79 ± 26 min. The approach to right ventricle to PA reconstruction and management of PA was a collegial decision left to each centre's medical and surgical staff, summarized in the flowchart in Fig. 1. From 2004 onwards, the LeCompte manoeuvre, described by Hraska [12], was performed when considered appropriate in 19 patients (28%). Surgical reduction of PA size, i.e. PA plasty, was performed by means of plication or excision of the PA wall in 36 patients (53%). Fifteen patients (22%) required delayed sternal closure.

Intensive care management after surgery and follow-up

Median intensive care unit stay was 6 days [interquartile range (IQR) 3–16]. PMV was defined, according to the literature, as postoperative ventilation for more than 7 days [13]. Early complications (defined as all complications occurring before the 30th postoperative day or hospital discharge if this occurred before the 30th day) were analysed. Postoperative airway compression

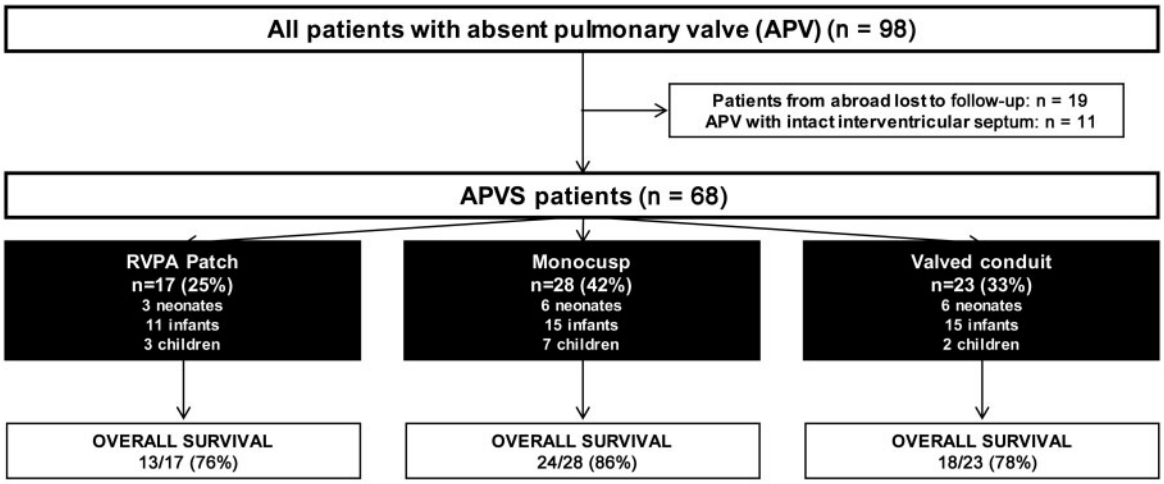


Figure 1: Flowchart of the entire cohort of patients with absent pulmonary valve syndrome (APVS); RVPA: right ventricle to pulmonary artery.

was assessed with CT scans and/or bronchoscopy records. All postoperative collected variables are summarized in Supplementary Material, Table S1. The last follow-up information, including clinical and echocardiographic data, was obtained from the referring senior cardiologist.

Statistical analysis

Descriptive analysis. All data were analysed with SPSS software (version 20, IBM, Chicago, IL, USA). Descriptive statistics for continuous variables are expressed as mean ± standard deviation or standard error of the mean when specified, whereas skewed continuous data are presented as median and IQR. Categorical variables are summarized as frequencies and percentages and compared using Pearson's χ^2 test or the Fisher's exact test if the expected value was less than 5. Continuous variables that were normally distributed were compared using Student *t*-tests and the analysis of variance. Skewed variables that deviated from a normal distribution were evaluated by non-parametric Mann–Whitney and Kruskal–Wallis tests. Multiple testing was performed for the analysis of the Nakata index between groups (Fig. 2) and for the analyses of mortality and PMV, including univariable analyses of risk factors for these outcomes and the effects of PA plasty and the LeCompte manoeuvre. *P*-values were corrected according to the Bonferroni method and with the Tukey *post hoc* procedure for analysis of variance.

Survival analysis. Early mortality was defined as death before 30 days after surgery. Kaplan–Meier actuarial survival curves were used to plot time-related end points for mortality using SPSS software. Differences between survival curves were evaluated with the log-rank statistic.

Univariable and multivariable regression analysis. Logistic regression was used to analyse risk factors for PMV, and Cox proportional hazards regression was used to determine time-related predictors of mortality. The proportional hazard assumption was tested graphically by plotting the log of the cumulative hazard functions against time and checking for parallelism, and by including an interaction term between the time and the studied variables in a time-dependent Cox model. Only preoperative variables with *P*-values <0.1 in univariable analyses were included in multivariable models for both outcomes. Supplementary Material, Table S1 shows candidate variables included in the models for mortality and PMV.

For multivariable mortality risk factors, a Lasso Cox model [14] was performed to select 2 variables of interest because of the low number of deaths. The 2 selected predictors were included in a bivariable Cox model. Multivariable PMV risk factors were analysed thanks to a backwards stepwise logistic regression model. Only preoperative variables with a *P*-value <0.1 in univariable analyses were included. SPSS software was used for all these analyses.

Receiver operating characteristics curves and cut-off analysis. Time-dependent receiver operating characteristic (ROC) curves for the ability of the Nakata index to predict mortality were constructed with SAS Studio (Version 3.6, The SAS Institute, Cary, NC, USA) at different time points until the date on which the last death occurred. SPSS Software was used for the ROC curve of the ability of the Nakata index to predict PMV. The area under the curve (AUC) and its 95% confidence interval (CI) were specified. Threshold cut-off values of the Nakata index were considered to be those providing the highest Youden index. A 2-tailed *P*-value <0.05 was considered statistically significant.

RESULTS

Clinical and surgical description and management

Sixty-eight patients were included. The median age at repair was 3.9 months (IQR 1.3–8.7), and the median weight was 5 kg (IQR 4–7). Table 1 summarizes preoperative characteristics of the whole cohort. Airway compression visualized by CT scan or bronchoscopy was more frequent at a younger age ($P = 0.012$) and more severe in neonates than in the other children (40% had moderate to severe compression vs 12% $P = 0.023$). Postoperative intensive care management according to age and preoperative airway compression is summarized in Supplementary Material, Table S2. Fifty-seven patients (84%) had at least 1 early postoperative complication, summarized in Supplementary Material, Table S3.

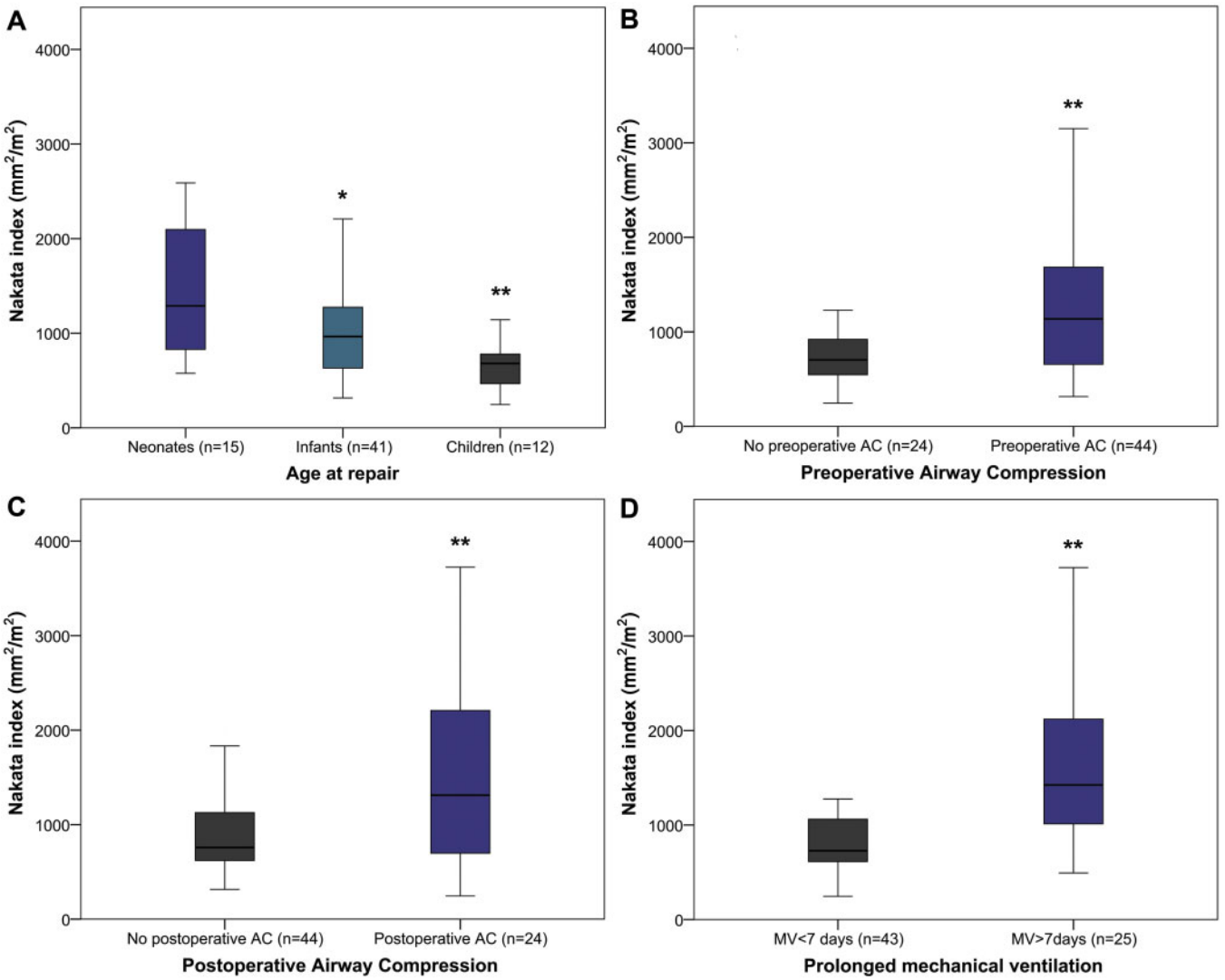


Figure 2: Nakata index distribution according to age at repair, airway compression and postoperative ventilation. (**A**) Box plots of Nakata index distribution according to age at repair; (**B**) according to preoperative airway status; (**C**) according to postoperative airway status; and (**D**) according to duration of postoperative mechanical ventilation. *Comparison between infants and children and **Comparison between neonates and children. *$P < 0.05$; **$P < 0.01$. AC: airway compression; MV: mechanical ventilation.

Association of pulmonary artery size expressed by the Nakata index with severity before and after repair

The median Nakata index was 938 mm^2/m^2 (IQR 625–1385). Patients with a younger age, preoperative or postoperative airway compression or requiring PMV had a significantly higher Nakata index (Fig. 2).

Mortality risk factors

Survival and predictors of mortality. The mortality rate at hospital discharge was 12% ($n = 8$), and the overall mortality rate was 19% ($n = 13$). Early deaths were mainly due to respiratory failure: 6 patients (46%) had refractory hypoxaemia leading to cardiac arrest and multiple organ failure; 1 had valved conduit thrombosis; and 1 died because of the decision to limit treatment secondary to ventilator dependency. Late deaths were also mainly due to respiratory failure secondary to pneumonia ($n = 3$); the other 2 died of causes not related to APVS. The overall mortality rate was 43% before 2005 and 17% in the recent decade (log-rank test $P = 0.187$).

Table 2 lists all preoperative variables associated with death in univariable analyses. These predictors of mortality were included in a Lasso Cox model. The paths of all coefficients of these variables are shown in Fig. 3A. A high Nakata index ($P < 0.001$) and a low basal SpO_2 ($P = 0.002$) were the 2 significant preoperative risk factors for mortality.

Ability of the Nakata index to predict time-dependent mortality. Figure 3B and C represent ROC curves of the ability of Nakata index to predict major outcomes. Time-dependent ROC curves of the ability of the Nakata index to predict mortality are presented in Fig. 3B. The AUC at 6 months had an excellent accuracy (AUC 0.92, 95% CI 0.85–0.99; $P = 0.010$), better than at other time-points. The cut-off value of the Nakata index to predict mortality at 6 months was 1500 mm^2/m^2, with a sensitivity of

98% and a specificity of 82%. Figure 4 shows Kaplan–Meier survival curves of patients according to their Nakata indexes. Survival was significantly better for patients with a Nakata index below 1500 mm^2/m^2.

Table 1: Preoperative characteristics of patients with absent pulmonary valve syndrome

	Patients ($n = 68$)
Demographic characteristics	
Simplified age at repair, *n* (%)	
Neonates	15 (22)
Infants	41 (60)
Children	12 (18)
Weight at birth (kg), mean ± SD	2.89 ± 0.73
Prematurity, *n* (%)	9 (13)
Prenatal diagnosis, *n* (%)	37 (54)
Gestational term, median (IQR)	30 (22–32)
22q11 deletion, *n* (%)	14 (21)
Respiratory status	
Basal SpO_2 (%), mean ± SEM	90.8 ± 1.3
Respiratory symptoms at repair[a], *n* (%)	53 (78)
Wheezing	18 (26)
Respiratory distress requiring oxygen therapy	17 (25)
Pulmonary infections	23 (34)
Atelectasis	9 (13)
Airway compression[b], *n* (%)	44 (65)
Localization of major compression[c], *n* (%)	
Trachea	6 (14)
Main bronchi	14 (32)
Left lobar bronchi	11 (25)
Right lobar bronchi	8 (18)
Distal airways	5 (11)
Need for invasive ventilation, *n* (%)	20 (29)
Age at ventilation (days), median (IQR)	0.5 (0–34)
Duration of ventilation (days), median (IQR)	5 (2–16)
Need for non-invasive ventilation, *n* (%)	13 (19)
Duration of NIV (days), median (IQR)	4 (1–6)

[a]Categories of respiratory symptoms are not exclusive.
[b]Airway compression was evaluated with chest radiographs and computed tomographic scans or bronchoscopy, with details on its localization and severity.
[c]Frequencies are expressed as percentages over the whole cohort ($n = 68$) except for the localization of major compression, expressed over the 44 patients with airway compression.
IQR: interquartile range; NIV: non-invasive ventilation; SD: standard deviation; SEM: standard error of the mean.

Risk factors for prolonged mechanical ventilation

Multivariable predictors of prolonged mechanical ventilation. The median duration of ventilation among the 25 patients requiring PMV was 15 days (IQR 11–38). Table 3 lists all preoperative variables associated with PMV in univariable and multivariable analyses. Only lower weight at repair emerged as a significant risk factor for PMV in multivariable analysis ($P = 0.008$). A higher Nakata index ($P = 0.079$) and a lower basal SpO_2 ($P = 0.052$) showed a trend towards PMV without reaching significance.

Ability of the Nakata index to predict prolonged mechanical ventilation. The accuracy of the Nakata index to predict PMV is presented in Fig. 3C. The AUC of the ROC curve was not as good as it was for survival (AUC 0.76, 95% CI 0.63–0.89; $P = 0.010$). The cut-off value was determined to be 1000 mm^2/m^2, with a sensitivity of 74% and a specificity of 71%.

Effects on outcomes of airway relief by pulmonary artery plasty and the LeCompte manoeuvre

Effects of pulmonary artery plasty and/or the LeCompte manoeuvre on mortality and prolonged mechanical ventilation. Patients with PA plasty alone or combined with the LeCompte manoeuvre had an increased risk of death (Table 4). Neither PA plasty nor the LeCompte manoeuvre had a protective effect on the duration of ventilation ($P = 0.17$ and $P = 0.10$, respectively).

Mortality and prolonged mechanical ventilation risk factors for patients with pulmonary artery plasty and/or the LeCompte manoeuvre. In patients who had the LeCompte manoeuvre, a higher Nakata index remained the only significant mortality risk factor (hazard ratio 1.001, 95% CI 1.0001–1.006; $P = 0.022$). The threshold Nakata index for mortality was 1637 mm^2/m^2, with a sensitivity of 75% and a specificity of 80%. In the group who had PA plasty, a Nakata index above 1564 mm^2/m^2 predicted mortality with a sensitivity of 86% and a specificity of 92%. None of the preoperative variables were significantly associated with PMV in the 2 groups.

Table 2: Preoperative risk factors for mortality in univariable and multivariable analyses

Variables	Survivors ($n = 55$)	Non-survivors ($n = 13$)	Univariable HR (95% CI)	*P*-value	Bivariable HR (95% CI)	*P*-value
Preoperative factors						
22q11 deletion, *n* (%)	8 (15)	6 (46)	3.8 (1.3–11.4)	0.024		
Preoperative invasive ventilation, *n* (%)	13 (24)	13 (100)	3.2 (1.1–9.5)	0.038		
Simplified age at repair (years)[b]	8; 35; 12	7; 6; 0	4.6 (1.7–12.5)	<0.001		
Weight at repair (kg)[a]	5 (4–7.5)	3 (3–4.5)	1.9 (1.2–3.2)	<0.001		
Nakata index (mm^2/m^2)[a]	798 (620–1184)	1915 (982–2571)	1.001 (1.0006–1.002)	<0.001	1.001 (1.001–1.002)	<0.001
Basal SpO_2 (%), mean ± SEM	91 ± 1.3	85 ± 3.7	1.04 (1.01–1.08)	0.018	1.06 (1.02–1.09)	0.002
Preoperative RVPA gradient (mmHg)[a]	73 (59–96)	60 (40–80)	1.03 (1.01–1.06)	0.045		

[a]Results are presented as medians (IQR) but continuous data were analysed.
[b]Simplified age at repair is categorized in 3 groups: neonates, infants and children. Respective numbers of patients in each group (number of neonates; infants; children) are presented according to mortality rate.
CI: confidence interval; HR: hazard ratio; IQR: interquartile range; RVPA: right ventricle to pulmonary artery; SEM: standard error of the mean.

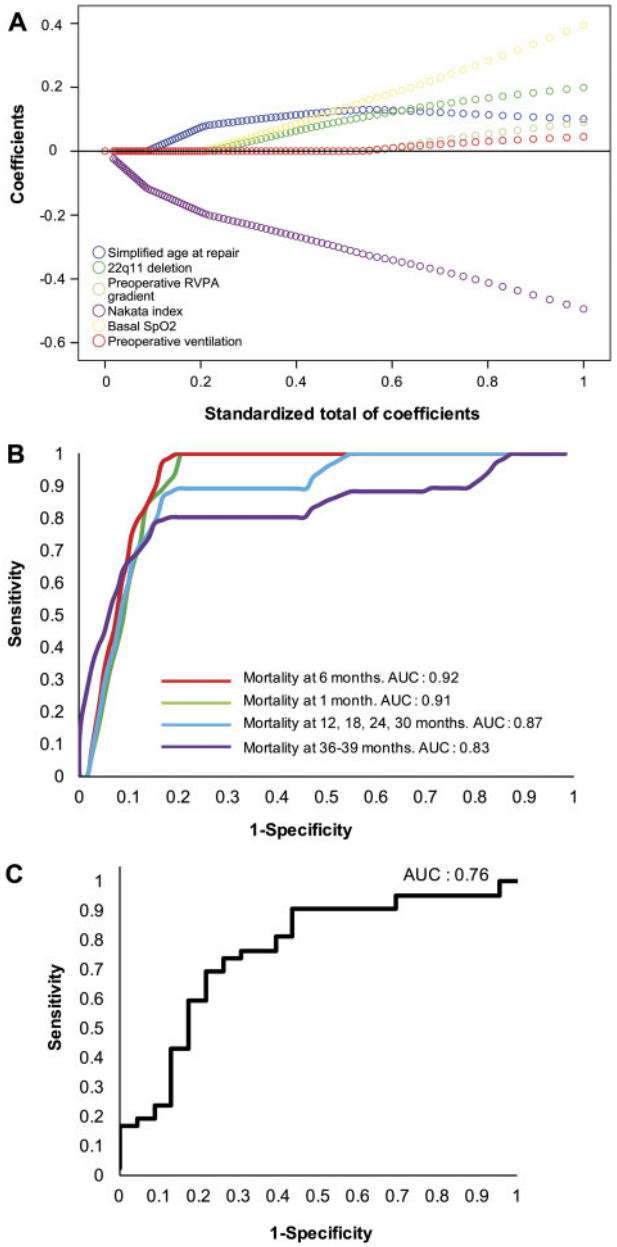


Figure 3: Ability of Nakata index to predict mortality and prolonged mechanical ventilation: Lasso Cox model for mortality and time-dependent ROC curves for mortality and prolonged mechanical ventilation. (**A**) Paths of coefficients of a Lasso regression plot for predictors of mortality. The 2 main predictors of mortality were the Nakata index and the basal SpO_2. (**B**) ROC curves for the accuracy of the Nakata index predicting mortality at 1, 6, 12, 18, 24, 30, 36 and 39 months. ROC curves were identical at time points in between which no event occurred. (**C**) ROC curve for the accuracy of the Nakata index predicting prolonged mechanical ventilation. AUC: area under the curve; ROC: receiver operating curve; RVPA: right ventricle to pulmonary artery.

Follow-up

Follow-up was complete in 93% (51/55 survivors), with a median follow-up time of 7 years (IQR 3.8–10.5). Twelve patients (23%) presented with respiratory symptoms during follow-up due to chronic respiratory failure ($n = 3$) or persistent wheezing with recurrent pulmonary infections ($n = 9$). Half of them had persistent obstructive and restrictive lung disease in pulmonary function tests. Two patients who had tracheostomy for ventilator dependency were weaned 2 years after the repair.

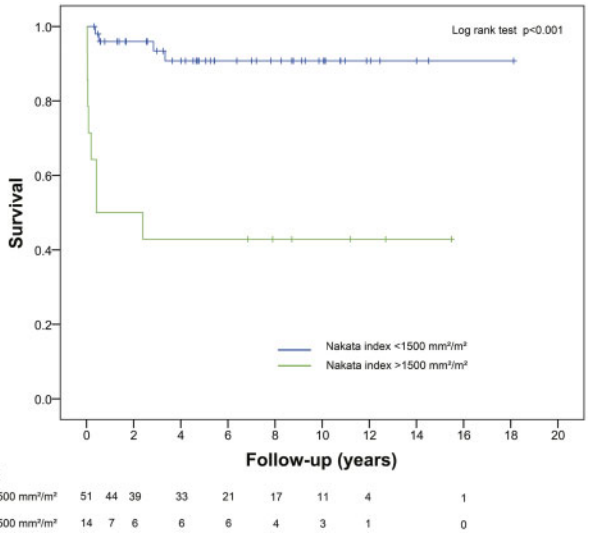


Figure 4: Survival curve according to a Nakata index above or below 1500 mm^2/m^2.

DISCUSSION

APVS remains a challenge because of significant and persistent airway compression. Reporting one of the biggest recent cohorts of this rare CHD, our study describes for the first time a threshold value of PA size that predicts mortality: indeed, a Nakata index above 1500 mm^2/m^2 predicts mortality at 6 months, with a sensitivity of 98% and a specificity of 82%. Lower weight at repair is the only significant multivariable PMV risk factor. Even in patients who had PA plasty or the LeCompte manoeuvre, a Nakata index above 1500 mm^2/m^2 remains predictive of mortality.

Our overall mortality rate of 19% was comparable to those of other contemporary series [15–17], as were our univariable mortality risk factors such as younger age at repair, weight <3 kg and preoperative ventilation [4–7, 18–20]. To our knowledge, the only mortality risk factor in multivariable analyses described to date was preoperative ventilation. In our study, multivariable risk factors were PA size (Nakata index) and basal SpO_2. These 2 factors emerged because they are direct but also better predictors of the severity of pulmonary disease in patients with APVS.

The challenge in APVS remains the management of the pulmonary disease. Indeed, PA dilatation induces not only extrinsic airway compression but also intrinsic abnormal lung function due to distal bronchial deformities and compression, beginning in the foetal period [21–23]. Resistance of small airways in APVS is known to be higher than that in patients with respiratory syncytial virus bronchiolitis, a typical small-airway disease [24]. Some authors tried to find a correlation between PA size side by side and outcome, without significant results [25, 26]. Our results show that PA size is directly correlated with the severity of this airway disease and that the description of PA size using the Nakata index was an accurate predictor of death related to respiratory failure, which occurs mostly within 6 months after repair.

Moreover, a large PA size with a Nakata index above 1500 mm^2/m^2 remained a mortality risk factor even in patients

Table 3: Preoperative risk factors for postoperative prolonged mechanical ventilation in univariable and multivariable analyses

Variables	MV <7 days (n = 43)	MV >7 days (n = 25)	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
Preoperative factors						
22q11 deletion, n (%)	5 (12)	9 (36)	4.3 (1.2–14.8)	0.023		
Airway compression, n (%)	22 (51)	22 (88)	7 (1.8–26.9)	0.005		
Preoperative invasive ventilation, n (%)	7 (16)	13 (52)	5.6 (1.8–17.2)	0.005		
Preoperative non-invasive ventilation, n (%)	5 (12)	8 (32)	3.6 (1.02–12.5)	0.048		
Simplified age at repair[b]	1; 30; 12	14; 11; 0	43.7 (5.4–352)	0.007		
Weight at repair (kg)[a]	6 (4.75–10.5)	4 (3–4)	3.0 (1.6–5.6)	<0.001	2.9 (1.3–6.7)	0.008
Nakata index (mm^2/m^2)[a]	733 (616–1101)	1424 (985–2145)	1.001 (1.001–1.002)	<0.001	1.001 (0.999–1.002)	0.079
Basal SpO_2 (%), mean ± SEM	94 ± 0.8	85 ± 2.9	1.13 (1.04–1.22)	<0.001	1.13 (1.00–1.28)	0.052
Preoperative RVPA gradient (mmHg)[a]	84 (65–100)	64 (48–76)	1.04 (1.01–1.07)	0.007		

[a]Results are presented as median (IQR) but continuous data were analysed.

[b]Simplified age at repair is categorized in 3 groups: neonates, infants and children. Respective numbers of patients in each group (number of neonates, infants and children) are presented according to duration of MV.

[c]Pearson's χ^2 test.

CI: confidence interval; IQR: interquartile range; MV: mechanical ventilation; OR: odds ratio; RVPA: right ventricle to pulmonary artery; SEM: standard error of the mean.

Table 4: Effects of pulmonary artery plasty and the LeCompte manoeuvre on principal outcomes

Variables	Survivors (n = 55), n (%)	Non-survivors (n = 13), n (%)	Univariable HR (95% CI)	P-value	MV <7 days (n = 43), n (%)	MV >7 days (n = 25), n (%)	Univariable OR (95% CI)	P-value
Surgical intervention								
PA plasty	25 (45)	11 (85)	5.8 (1.3–26.2)	0.019	20 (46)	16 (64)	2.0 (0.7–5.6)	0.168
LeCompte manoeuvre	15 (27)	4 (31)	1.2 (0.4–4.1)	0.712	9 (21)	10 (40)	2.5 (0.8–7.5)	0.101
PA plasty and LeCompte manoeuvre	5 (9)	4 (31)	4.1 (1.2–13.3)	0.022	5 (12)	4 (16)	2.4 (0.6–10.1)	0.224

CI: confidence interval; HR: hazard ratio; MV: mechanical ventilation; OR: odds ratio; PA: pulmonary artery.

who benefited from interventions to mechanically relieve proximal airway compression such as PA plasty or the LeCompte manoeuvre. This is probably because the decision to provide mechanical relief in these patients was related to their PA size, which is also a marker of the severity of intrinsic airway disease. We believe that PA plasty or the LeCompte manoeuvre is essential to treat proximal airway compression as described in the literature [12, 27] but may not effectively relieve distal bronchi compression.

Only Yong *et al.* [7] showed that preoperative ventilation and operation during infancy were risk factors for PMV. We found only lower weight to be a significant multivariable PMV risk factor. Factors leading to PMV following cardiac surgery are multiple and complex [28, 29], and lower weight might be a better surrogate parameter accounting for this complexity than the Nakata index, mostly reflecting the severity of airway disease that occurs in the neonatal period or in early infancy.

Limitations

We used the Nakata index as a novel approach to describe PA size. However, the Nakata index [11] was validated only in patients with CHD and small PAs. PA size was measured only by echocardiography in 40% of our cohort. Still, echocardiographic measurements have a fair agreement with angiographic measurements of PA size in normal or enlarged PAs [30]. To ensure that the data are compatible with recent management protocols, PA size may nowadays be evaluated with CT scans. Nevertheless, measurement of PA size by echography could be useful for diagnostic cardiologists to generate a prognosis, delay the need for CT scanning in low-risk populations and provide timely information for families.

Mortality and other subgroup analyses were based on a relatively small number of events. Certainly, PA size is a good predictor of outcome and could be used for prognosis in this disease, but all risk factors, such as lower weight, the presence of respiratory symptoms during the neonatal period and the decision to reduce the size of the PA or perform a LeCompte manoeuvre, are interrelated.

CONCLUSION

AVPS is a rare CHD with a severe respiratory disease due to compression of large and small airways secondary to dilatation of the PAs because of the absence of pulmonary leaflets. We showed that preoperative assessment of the Nakata index before repair was accurately able to predict mortality, with a critical value of 1500 mm^2/m^2. Above this threshold, a risk of death persists even after an intervention for airway relief such as PA size reduction or the LeCompte manoeuvre. Stratification of patient risk according to PA size may help to organize timely repair, to better define patients at risk for airway compression and to manage postoperative ventilation.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Conflict of interest: none declared.

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