Original Article

Adverse events after repair of tetralogy of Fallot: prediction models by machine learning of a retrospective cohort study in western China

Linyun Xi[1,2], Ming Xiang[1,2], Chun Wu[1,2], Zhengxia Pan[1,2], Jiangtao Dai[1,2], Gang Wang[1,2], Hongbo Li[1,2], Yong An[1,2], Yonggang Li[1,2], Yuan Zhang[1,2], Xiaoqin Wei[1,2], Dawei He[2,3], Quan Wang[1,2]

[1]Department of Cardiothoracic Surgery, Ministry of Education Key Laboratory of Child Development and Disorders, National Clinical Research Center for Child Health and Disorders, China International Science and Technology Cooperation Base of Child Development and Critical Disorders, Children's Hospital of Chongqing Medical University, Chongqing, China; [2]Ministry of Education Key Laboratory of Child Development and Disorders, National Clinical Research Center for Child Health and Disorders, China International Science and Technology Cooperation Base of Child Development and Critical Disorders, Chongqing Key Laboratory of Pediatrics, Children's Hospital of Chongqing Medical University, Chongqing, China; [3]Department of Urology, Ministry of Education Key Laboratory of Child Development and Disorders, National Clinical Research Center for Child Health and Disorders, China International Science and Technology Cooperation Base of Child Development and Critical Disorders, Children's Hospital of Chongqing Medical University, Chongqing, China

Contributions: (I) Conception and design: D He, L Xi, M Xiang, Q Wang; (II) Administrative support: D He; (III) Provision of study materials or patients: C Wu, Z Pan, J Dai, G Wang, H Li, Y An, Y Li; (IV) Collection and assembly of data: L Xi, M Xiang, Q Wang, Y Zhang, X Wei; (V) Data analysis and interpretation: L Xi, Q Wang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Quan Wang. No. 136, Zhongshan 2nd Road, Yuzhong Dis., Chongqing 400014, China. Email: 1024068781@qq.com.

Background: The incidence of clinical adverse events after tetralogy of Fallot (TOF) repair remains high. This study was performed to explore risk factors for adverse events and develop a prediction model through machine learning (ML) to forecast the incidence of clinical adverse events after TOF repair.

Methods: A total of 281 participants who were treated with cardiopulmonary bypass (CPB) at our hospital from January 2002 to January 2022 were included in the study. Risk factors for adverse events were explored by composite and comprehensive analyses. Five artificial intelligence (AI) models were used for ML to build prediction models and screen out the model with the best performance in predicting adverse events.

Results: CPB time, differential pressure of the right ventricular outflow tract (RVOTDP or DP), and transannular patch repair were identified as the main risk factors for adverse events. The reference point for CPB time was 116.5 minutes and that for right ventricular (RV) outflow tract differential pressure was 70 mmHg. SPO_2 was a protective factor, with a reference point of 88%. By integrating the results for the training and validation cohorts, we confirmed that, among all models, the logistic regression (LR) model and Gaussian Naive Bayes (GNB) model were stable, showing good discrimination, calibration and clinical practicability. The dynamic nomogram can be used as a predictive tool for clinical application.

Conclusions: Differential pressure of the RV outflow tract, CPB time, and transannular patch repair are risk factors, and SPO_2 is a protective factor for adverse events after complete TOF repair. In this study, models developed by ML were established to predict the incidence of adverse events.

Keywords: Tetralogy of Fallot (TOF); artificial intelligence (AI); machine learning (ML); adverse events

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Introduction

Tetralogy of Fallot (TOF) is the most common cyanogenic congenital heart disease, accounting for approximately 10% of all congenital heart diseases. Early surgical repair in the first year of life is now commonly performed at most major centres. Intraoperative mortality is less than 2% to 3% when the repair is performed at an early age (1). Peritoneal dialysis and pneumonia, with a reported incidence of 62.4% (2), are still common and have become important factors that often prolong the length of hospital stay and increase expenses (3), imposing a heavy burden on society and families. In developing areas, such as western China, many patients undergo surgery after the optimal period. The mortality rate and incidence of postoperative adverse events are higher in these areas than in developed areas, just as the intraoperative mortality rate is higher in developing countries than in developed countries (1). Surgeons should make more of an effort to help parents understand the disease severity and inform them of the varying probability of complications among patients. Moreover, due to the slow spread of medical information, parents are often anxious, doubt the treatment and become argumentative when their children experience adverse events. Hence, an accurate and reliable preoperative predictive model of adverse events would be very meaningful not only for individualized treatment but also for communication between the surgeons and parents.

With the widespread application of artificial intelligence (AI) in the medical field, machine learning (ML) has rendered medical research involving prediction models more scientific and practical (4,5); however, we note that in the area of TOF, this kind of research is scarce. Therefore, we combined AI with basic clinical metrics and echocardiography to provide an accurate and reliable prediction model for clinical work. We present the following article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-246/rc).

Highlight box

Key findings

- Differential pressure of the right ventricular outflow tract, cardiopulmonary bypass time, and transannular patch repair are risk factors, and SPO_2 is a protective factor for adverse events after complete tetralogy of Fallot repair.

What is known and what is new?

- The reference point was 116.5 minutes of CPB time, 88% of SPO_2 and the reference point of differential pressure of the right ventricular outflow tract cutoff was 70 mmHg.

What is the implication, and what should change now?

- Patients should receive individualized treatment according to the patients different condition.

Methods

Data and patients

Clinical data for patients with TOF who underwent anatomical correction from January 2002 to January 2022 were collected. All patients underwent computed tomography angiography (CTA) and echocardiography. Patient characteristics, such as weight and age, pulmonary venous anatomy, demographics, preoperative data, intraoperative data, postoperative data and adverse events, were recorded.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the ethics committee of our hospital (Approval No. 2021-352), and informed consent was obtained from all patients' parents or legal guardians.

All patients included were diagnosed with TOF (ICD-10: Q21.3) and underwent standard primary complete repair (ICD-9-CM-3: 35.81). Patients were excluded if (I) they also had pulmonary atresia, major aortopulmonary collateral arteries, or an atrioventricular (AV) septal defect; (II) they had undergone palliative procedures, such as right ventricular (RV) outflow ballooning/stenting or arterial duct stenting; or (III) they had undergone staged repair with unifocalization of the pulmonary arteries and conduit placement subsequently followed by ventricular septal defect (VSD) closure.

Definition and predictors

Adverse events included arrhythmia, peritoneal dialysis, pneumonia, and death occurring before discharge. Arrhythmia involved complete AV blockage requiring pacemaker implantation and ventricular tachycardia or supraventricular tachycardia and other arrhythmias requiring treatment. Pneumonia was defined as pneumonia developing at 48 hours or more after the initiation of mechanical ventilation, including both of the following criteria: fever (body temperature greater than 38.5 ℃) and positive cultures of sputum obtained by suction. The indications for peritoneal dialysis were as defined by Baskin (6).

Age, sex, weight, pulmonary valve annulus Z score (Z-index), transannular patch repair (TP repair), preoperative SPO_2, aortic cross-clamp (ACC) time, cardiopulmonary bypass (CPB) time, opening of the pulmonary valve (PvO), differential pressure of the right ventricular outflow tract (RVOTDP or DP), pulmonary valve leaflet (PV-leaflet; two or three), annulus of the pulmonary artery (annulus), VSD size, left ventricular end-diastolic volume index (LVEDI), haematocrit (HCT), ejection fraction (EF), McGoon index (M-index), and lateral branch occlusion (branch occlusion) were used as predictors. In addition, the surgical team and the year the surgery was performed were analysed to avoid potential bias. However, these factors were not included in the models because they could not be used as available predictors.

Surgical technique

All patients underwent surgery with a standard median sternotomy and CPB. A Gore-Tex patch was used to close the VSD, and the right ventricular outflow tract (RVOT) was dredged according to the pulmonary artery anatomy (3). The pulmonary valve annulus was preserved if a Hegar bougie of the appropriate size could be passed smoothly after supravalvular and subvalvular stenoses were completely removed. If a Hegar bougie one size lower than the appropriate size could be passed and the RV/left ventricular (LV) pressure ratio (RV pressures were measured by direct needle puncture) was above 0.7, TP repair was performed.

Statistical analysis

Means and standard deviations (SDs) are used to display continuous data. The Shapiro-Wilk test was used to evaluate the normality of distributions, and an unpaired *t*-test was used to compare continuous variables between two groups. The Mann-Whitney U test was used to compare data for variables without a normal distribution. Data for categorical variables were compared by the chi-square test. Standardized differences less than 0.10 indicated an absolute balance (7). A multiple collinearity test was used to remove confounding variables, and least absolute shrinkage and selection operator (LASSO) regression was utilized to rank the importance of predictors. Univariate logistic regression (LR) and subgroup analyses were used in this study. The variables confirmed by the univariate LR, LASSO regression and subgroup analyses were selected as the main variables affecting the occurrence of adverse events and further analysed by propensity score matching (PSM), trend analysis and restricted cubic spline (RCS) analysis.

In the ML model, LR, Gaussian Naive Bayes (GNB), multilayer perceptron (MLP), support vector machine (SVM) and K-nearest neighbour (KNN) were chosen, and R version 3.6.3 and Python version 3.7 were used to analyse statistics. More detailed parameter settings are provided in Table S1. The whole dataset was randomly divided into training and test sets at a ratio of 4:1. The guidelines of the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) Initiative were used to report the risk prediction model (8). A receiver operating characteristic (ROC) curve was used to analyse the discrimination of each model. A comprehensive assessment by the area under the curve (AUC) of the training and test sets was performed to select the most reliable model and avoid overfitting. The Hosmer-Lemeshow test was used to identify the most reliable model (9). A Brier score less than 0.25 was considered to indicate that a model had good comprehensive properties. A formula and a dynamic nomogram that could exhibit the clinical application of the model were provided on a web page, and the clinical utility of the model was evaluated by decision curve analysis (DCA) (10).

Results

The flow chart of the study is shown in *Figure 1*. A total of 281 participants were included, with adverse events occurring in 131 of them. The variance of all variables was less than 10. Hence, all the variables passed the multiple collinearity test. Nearly ninety percent of the patients with adverse events underwent TP repair; the integrity of the pulmonary valve was preserved in one-third of patients with no adverse events (P=0.01). Differences in SPO_2, CPB time, age, PvO, DP, annulus, M-index, Z-index, TP repair and LVEDI were observed between the two groups. Only the distributions of branch occlusion and HCT were well balanced (*Table 1*). Significant differences in DP (P=0.003), CPB time (P=0.016), sex (P=0.047), TP repair (P=0.037) and SPO_2 (P=0.001) were detected by univariate LR (*Table 2*). Significant differences in the year of surgery [odds ratio (OR) =0.938–1.021, P=0.325] and surgical team (OR =0.379–2.156, P=0.827) were not observed. The order of feature importance was SPO_2, DP, CPB, TP repair, sex, age, etc. (*Figure 2*). The detailed variables of feature importance are shown in Table S2. The minimum criterion lambda had a value of 0.058, showing that excessive convergence

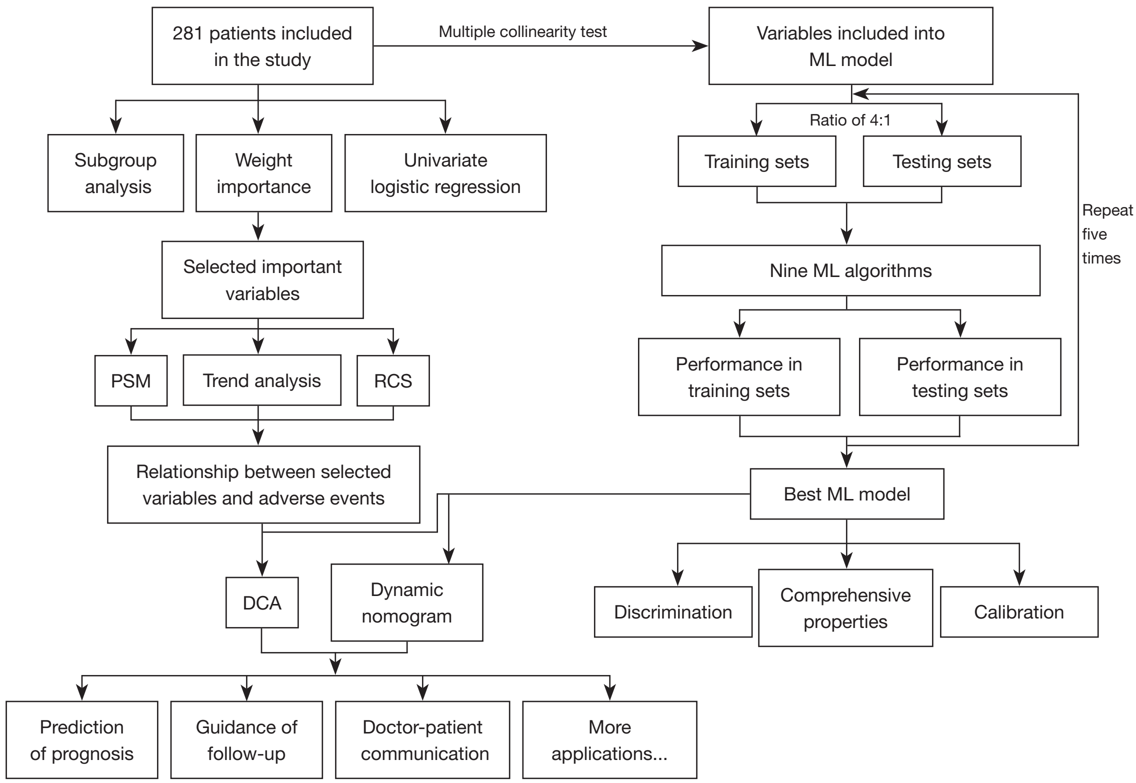

Figure 1 Flow chart of the study. PSM, propensity score matching; RCS, restricted cubic spline; ML, machine learning; DCA, decision curve analysis.

would not occur when analysing no more than 6 variables in detail (*Figure 3*). A Venn diagram was used to select the main variables according to the three analytical methods mentioned above, resulting in the selection of SPO_2, CPB time, DP, and TP repair (*Figure 4*).

CPB time and DP were identified as the main risk factors for adverse events. The reference point [hazard ratio (HR)/OR =1] was 116.5 minutes of CPB time or 70 mmHg of DP (*Figure 5*). The results indicated that the risk of adverse events would significantly increase with a CPB time longer than 116.5 minutes or a DP higher than 70 mmHg. SPO_2 was a protective factor, with a reference point of 88% (*Figure 5*).

Sixty-three patients were included in the TP repair group and pulmonary valve preservation group after PSM (available online: https://cdn.amegroups.cn/static/public/tp-22-246-1.xlsx). The incidence of adverse events in the TP repair group was slightly higher than that in the pulmonary valve preservation group [(30/63) 47.6% *vs.* (20/63) 31.7%, P=0.07].

We also performed a trend analysis to observe whether different TP repair strategies would influence adverse events in different SPO_2 groups (*Figure 6*). The results show that pulmonary valve preservation can reduce the incidence of adverse events at any oxygen saturation.

According to the principle of AI models, we included all variables in model construction. The best-performing models for the training set were the LR model and GNB model, with mean AUCs of 0.760 and 0.730, respectively. The performances of the LR model and GNB in the test set were also good, with mean AUCs of 0.701 and 0.707, respectively (*Figure 7*). The details of the five testing processes are shown in Tables S3,S4.

Next, we focused on the LR model. To analyse the discrimination capability of the model, we performed a detailed analysis of the individual LR model. The specificity, sensitivity and accuracy were 0.716, 0.732 and 0.721, respectively, and the AUC was 0.760. Therefore, the discrimination of the model was good (Figure S1).

Model calibration was evaluated by the Hosmer-Lemeshow test (Figure S2). No significant difference was found between the observed and expected values (mean

Table 1 Demographic and preoperative clinical characteristics

Variable	Adverse event (n=131)	Non-adverse event (n=150)	P value	Standardized differences
Gender, n	Male/female (88/43)	Male/female (85/65)	0.08	0.22
Age (months), median (IQR)	12 (8.0–17.0)	12 (8.0–25.0)	<0.001*	0.73
Weight (kg), median (IQR)	8.9 (7.5–10)	9 (7.0–10.6)	0.09	0.20
HCT (%), median (IQR)	42.8 (37.9–48.7)	40.75 (36.78–45.78)	0.71	0.04$^{\Delta}$
SPO_2 (%), median (IQR)	84 (75–91)	89 (81.75–95.00)	<0.001*	0.52
CPB-time (min), median (IQR)	119 (106–140)	113 (98.75–128.0)	0.01*	0.69
ACC-time (min), median (IQR)	78 (68–87)	75 (65–86.25)	0.06	0.19
EF (%), median (IQR)	64 (61–69)	66 (61–71)	0.25	0.14
VSD (mm), median (IQR)	13.5 (12–15)	13.30 (12.0–15)	0.46	0.10
Z-index, median (IQR)	−1.82 (−2.75, −1.26)	−1.46 (−2.4, −0.22)	0.01*	0.67
M-index, median (IQR)	1.38 (1.23–1.64)	1.50 (1.28–1.71)	0.04*	0.52
LVEDI (mL/m^2), median (IQR)	41.76 (33.49–53.05)	49.80 (37.36–59.48)	0.01*	0.35
PvO (cm), median (IQR)	4.7 (3.7–5.4)	5.0 (4.1–6.2)	<0.001*	0.47
DP (mmHg), median (IQR)	71 (60–86)	65 (55–81)	<0.001*	0.83
Annulus (cm), median (IQR)	9.2 (7.8–10.0)	10.0 (8.5–12.0)	<0.001*	0.48
PV-leaflet, n	Yes/no (50/81)	Yes/no (54/96)	0.71	0.23
TP-repair, n	Yes/no (115/16)	Yes/no (103/47)	0.01*	0.46
Branch occlusion, n	Yes/no (10/121)	Yes/no (12/138)	0.99	0.01$^{\Delta}$

*, P<0.05; $^{\Delta}$, standardized differences less than 0.10 indicated absolute balance. IQR, interquartile range; HCT, haematocrit; CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; EF, ejection fraction; VSD, ventricular septal defect; Z-index, pulmonary valve annulus Z score; M-index, McGoon index; LVEDI, left ventricular end-diastolic volume index; PvO, opening of the pulmonary valve; RVOTDP or DP, differential pressure of the right ventricular outflow tract; PV-leaflet, pulmonary valve leaflet; TP repair, transannular patch repair.

absolute error =0.061). Furthermore, the model showed good comprehensive performance, with a Brier score of 0.129. Coefficients of variables were used to construct a nomogram (*Figure 8*) to predict adverse events after radical correction of TOF. The dynamic nomogram can be used online (https://ml-cqmu.shinyapps.io/DynNomapp-TOF/), and the detailed parameters of the model can also be found on this webpage.

SPO_2 and TP repair were important parameters according to the clinical application and analysis in our study. Hence, DCA was performed for the adverse events and showed that the model combined with SPO_2 and TP repair promotes clinical decision making (*Figure 9*).

Discussion

Adverse events require additional drug intervention, with some of them even necessitating reoperation, which greatly increases surgical trauma to the patient and prolongs the ICU or hospital stay. However, we still have little knowledge regarding the related issues, such as the risk factors for adverse events and the cut-off points of such risk factors. With such unanswered questions, we chose the above complications as assessment criteria and constructed a prediction model.

Considering that a model to predict adverse events is urgently needed, we collected the clinical data of 281 children. After screening, we successfully constructed 5 prediction models using various AI methods. The LR model and GNB model were found to have relatively stable performances in both the training set and the test set. Since the algorithm of the LR model is simpler and easy for clinicians to use, we paid more attention to the detailed performance of the LR model. The LR model was evaluated by cross validation, ROC analysis, calibration curves, and DCA. As the predictors used in our study are

Table 2 Univariate logistic regression of adverse event

Factors	OR	95% CI (lower)	95% CI (higher)	P value
Annulus	0.915	0.651	1.255	0.549
DP	1.024	1.008	1.04	0.003*
PvO	0.947	0.742	1.199	0.655
LVEDI	1.003	0.987	1.019	0.683
M-index	1.036	0.453	2.381	0.933
Z-index	1.027	0.668	1.625	0.899
VSD	1.055	0.942	1.184	0.356
EF	0.971	0.926	1.017	0.212
ACC-time	0.974	0.944	1.003	0.084
CPB-time	1.025	1.005	1.046	0.016*
SPO_2	0.949	0.92	0.978	0.001*
HCT	0.998	0.974	1.012	0.757
Weight	0.986	0.817	1.189	0.879
Age	0.986	0.957	1.015	0.324
PV-leaflet	1.184	0.677	2.076	0.554
Gender	1.757	1.013	3.085	0.047*
TP-repair	2.193	1.063	4.68	0.037*
Branch occlusion	0.966	0.338	2.704	0.948

*, P<0.05. OR, odds ratio; CI, confidence interval; RVOTDP or DP, differential pressure of the right ventricular outflow tract; PvO, opening of the pulmonary valve; LVEDI, left ventricular end-diastolic volume index; M-index, McGoon index; Z-index, pulmonary valve annulus Z score; VSD, ventricular septal defect; EF, ejection fraction; ACC, aortic cross-clamp; CPB, cardiopulmonary bypass; HCT, haematocrit; PV-leaflet, pulmonary valve leaflet; TP repair, transannular patch repair.

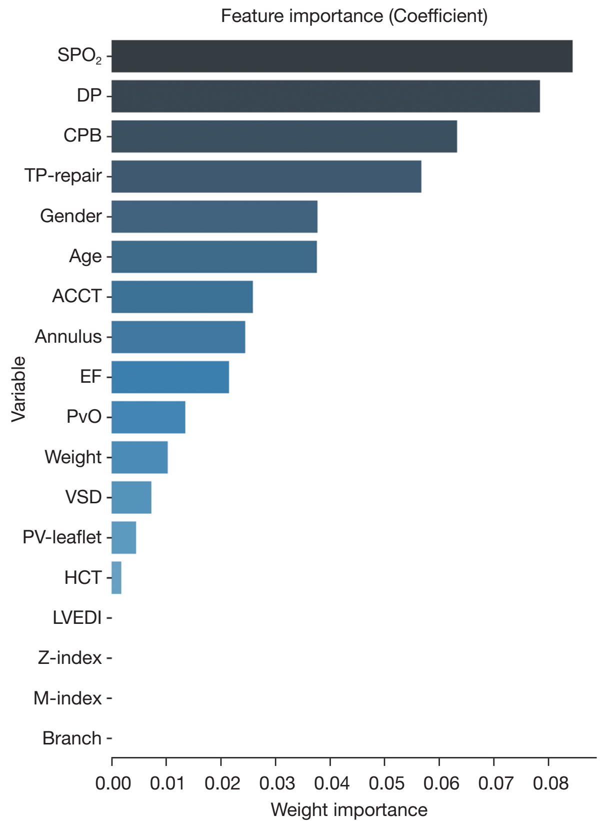

Figure 2 Coefficients of importance. RVOTDP or DP, differential pressure of the right ventricular outflow tract; CPB, cardiopulmonary bypass; TP repair, transannular patch repair; ACCT, Aortic cross-clamp time; EF, ejection fraction; PvO, opening of the pulmonary valve; VSD, ventricular septal defect; PV-leaflet, pulmonary valve leaflet; HCT, haematocrit; LVEDI, left ventricular end-diastolic volume index; Z-index, pulmonary valve annulus Z score; M-index, McGoon index.

available at the completion of surgery, prediction using this model can be carried out early, without a long follow-up time. To our knowledge, this is the first model to use AI for the prediction of adverse events in cases of TOF. This model can guide better preoperative evaluations of patients' conditions.

Early repair of TOF is generally advised to alleviate myocardial fibrosis and mitochondrial damage to myocardial cells, which result from long-term anoxia and correlate positively with SPO_2 and the pressure of the RVOT (11-13). Studies have reported the timing of the repair in a large cohort of infants and found the optimal age to be between 3 and 11 months (14,15). Despite this, patients are individuals, and different patients have different disease conditions. Not all patients will be suitable for the same surgical strategy or undergo surgery at the same age, especially in Chongqing, a city in western China with less-developed medical technology. Thus, some objective and definite predictors are needed to narrow the age at surgery.

In the past, parents may have found it difficult to choose an appropriate time for their child to undergo surgery. With the help of this prediction model, the SPO_2 and RVOT pressure cut-off points can be used to divide patients into high-risk (e.g., SPO_2 lower than the cut-off point) and low-risk (e.g., SPO_2 higher than the cut-off point) groups preoperatively. For patients whose preoperative SPO_2 is higher than 88% or whose RVOT pressure is lower than 70 mmHg, parents can be advised based on evidence that an older age (such as older than 6 months), at which CPB is more tolerable, would be more suitable for the surgery. For patients whose preoperative SPO_2 is lower than 88% or whose RVOT pressure is higher than 70 mmHg, a younger age would be recommended to alleviate myocardial fibrosis and mitochondrial damage to myocardial cells.

With the help of this model, better communication with patients can be conducted preoperatively, allowing parents to understand the rate of adverse events and the severity of disease. Due to the complex haemodynamics of TOF, communication with parents regarding haemodynamics and cardiac abnormalities may not resolve their concerns; thus, a more effective method is needed. This model offers visualization and is concrete, making the information easier to understand. More accurate data also allow for improved trust during communication.

Analysis of risk factors for postoperative adverse events can guide the medical community to improve surgical strategies, avoid, minimize or even eliminate risk factors, and ultimately reduce the incidence of adverse events. For example, to decrease the CPB time, if a monocusp is needed for TP repair, another group of surgeons would perform this work during the operation. Based on our findings, TP repair should be carefully selected during the operation, and the pulmonary annulus should be retained as much as possible. For patients whose pulmonary annulus may be destroyed, monocusps are strongly recommended, and the RV/LV pressure ratio should also be considered.

Unsurprisingly, preoperative SPO_2 and RVOT pressure were risk factors. Hypoxia and RVOT obstruction lead to pathological changes such as RV hypertrophy and myocardial interstitial fibrosis (16). Chronic hypoxia is a major stimulus for myocardial remodelling and causes

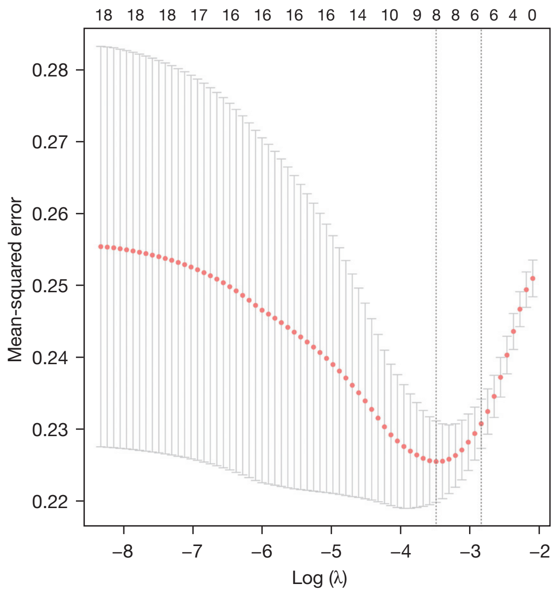

Figure 3 Coefficients of the LASSO model: LASSO coefficient profiles of the 6 features. A coefficient profile plot was produced against the log λ sequence. LASSO, least absolute shrinkage and selection operator.

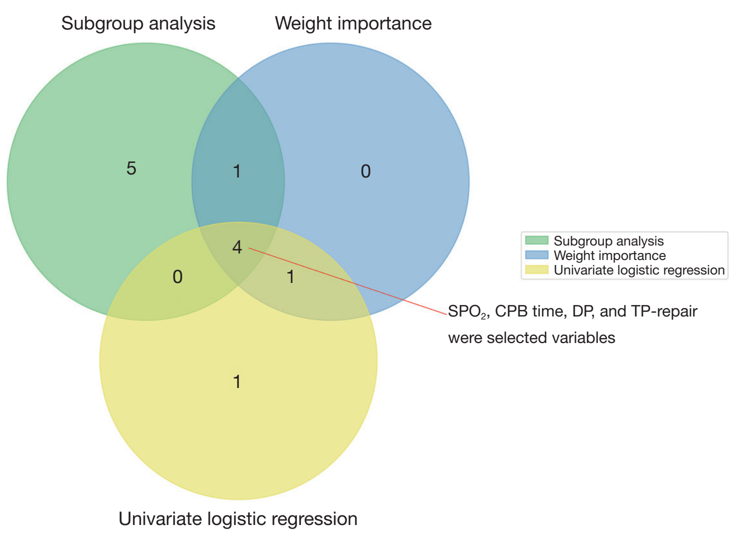

Figure 4 Venn diagram of the variables selected according to the three analytical methods mentioned above. CPB, cardiopulmonary bypass; RVOTDP or DP, differential pressure of the right ventricular outflow tract; TP repair, transannular patch repair.

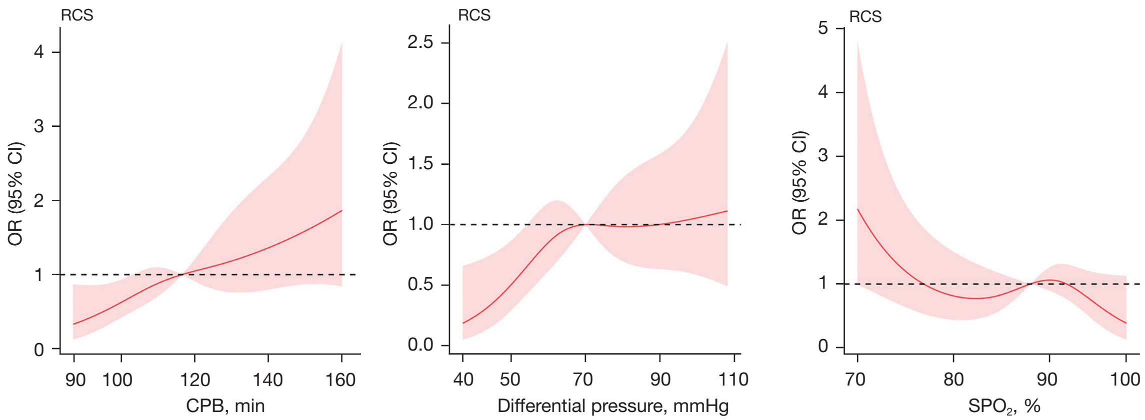

Figure 5 RCS analysis of CPB time, DP and SPO_2 according to adverse events. The reference points (HR/OR =1) were 116.5 minutes for CPB time, 88% for SPO_2 and 70 mmHg for DP. OR, odds ratio; CI, confidence interval; RCS, restricted cubic spline; CPB, cardiopulmonary bypass; DP, differential pressure of the right ventricular outflow tract; HR, hazard ratio.

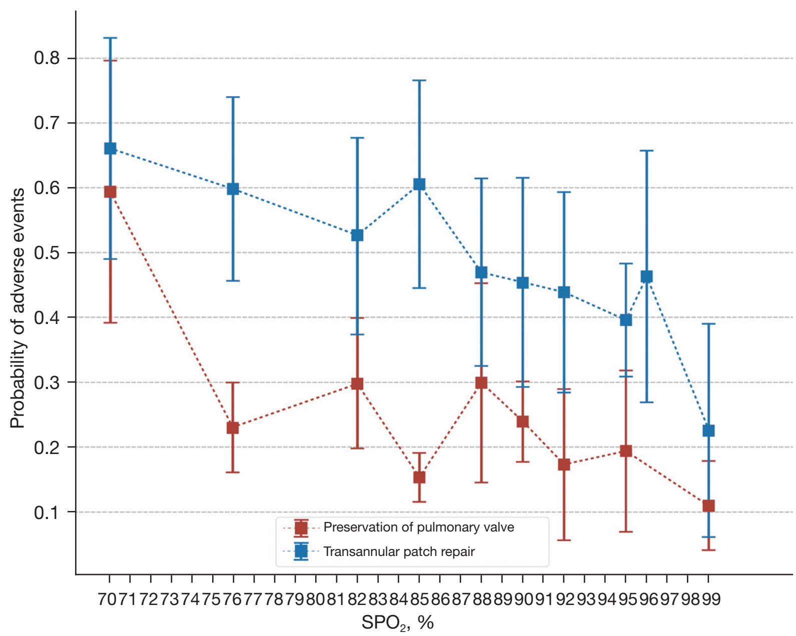

Figure 6 Trend analysis between different TP repair strategies and adverse events over SPO_2. TP, transannular patch.

detrimental histopathological alterations in cardiac myocytes and fibrosis (13,17). Previous studies have shown varying degrees of histopathological changes and mild fibrosis in muscle specimens from TOF patients (11,18). Some studies found the function of both the left and right ventricles to be damaged (19), which is also believed to be related to myocardial fibrosis (20). Notably, TP repair can lead to pulmonary regurgitation (PR), inducing RV volume overload and often progressive RV dilation, which may include the development of tricuspid regurgitation and RV dysfunction.

In addition, we analysed the influences of the year in which the surgery was conducted and differences in the surgical team on the outcome. The results showed that the year in which surgery was conducted and differences in the surgical team did not influence the outcome. The reasons for these findings might be as follows: firstly, all the patients underwent standard primary complete repair, and the

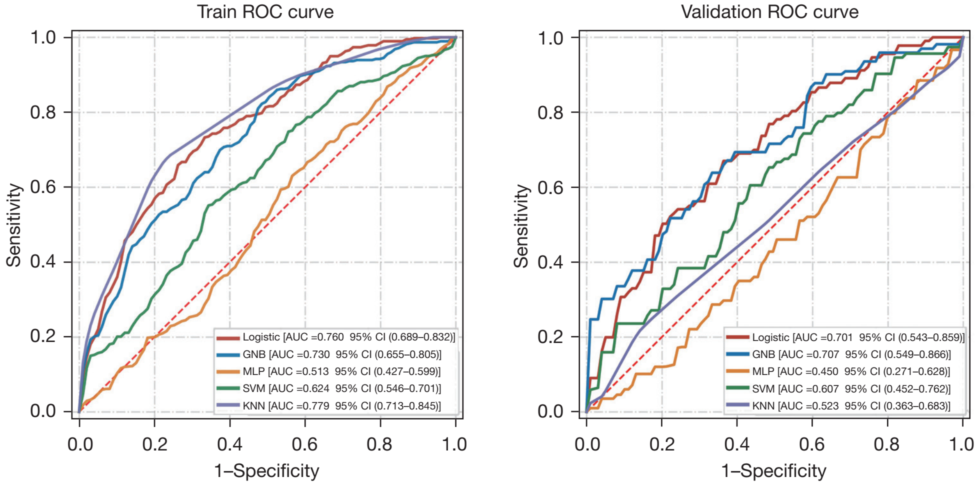

Figure 7 Predicted ROC curve of adverse events in the training and testing sets of the five models. ROC, receiver operating characteristic; AUC, the area under the curve; CI, confidence interval; GNB, Gaussian Naive Bayes; MLP, multilayer perceptron; SVM, support vector machine; KNN, K-nearest neighbour.

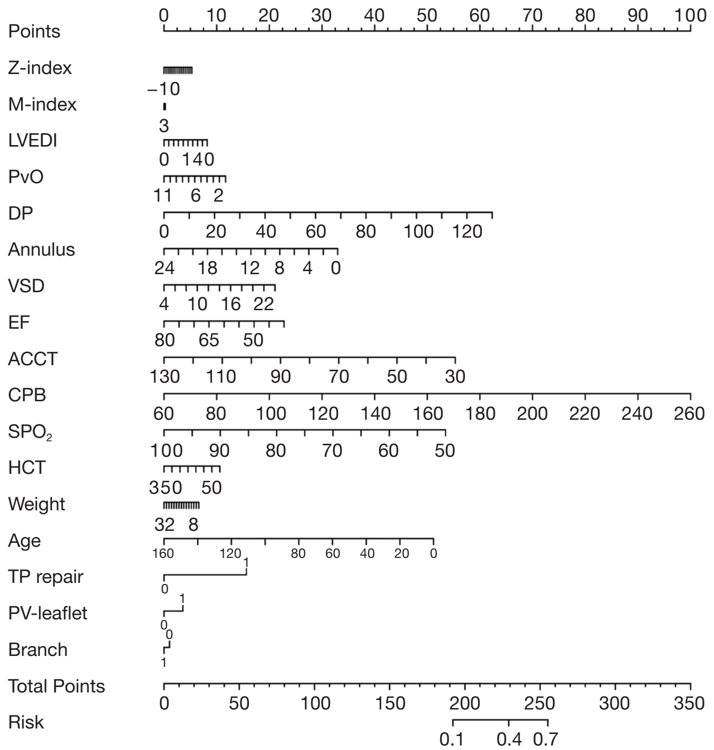

Figure 8 Nomogram of the LR model for adverse events. To estimate the probability for an individual patient, the value of each factor is acquired on each variable axis; then, a line is drawn upwards to determine the point. The sum of these numbers is located on the total points axis, and a line is drawn downwards to the risk axis to determine the likelihood of an adverse event. Z-index, pulmonary valve annulus Z score; M-index, McGoon index; LVEDI, left ventricular end-diastolic volume index; PvO, opening of the pulmonary valve; RVOTDP or DP, differential pressure of the right ventricular outflow tract; VSD, ventricular septal defect; EF, ejection fraction; ACCT, aortic cross-clamp time; CPB, cardiopulmonary bypass; HCT, haematocrit; TP repair, transannular patch repair; PV-leaflet, pulmonary valve leaflet; LR, logistic regression.

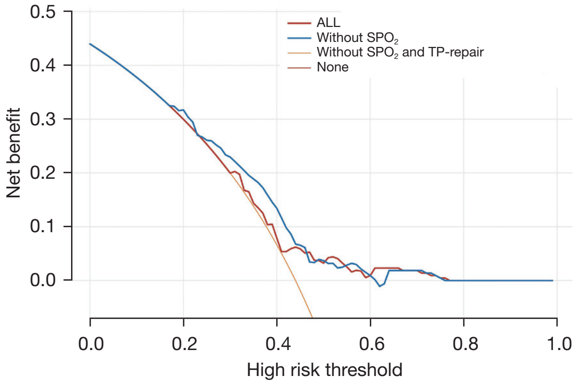

Figure 9 DCA for the model combining SPO_2 and TP repair. The y-axis measures the net benefit. TP repair, transannular patch repair; DCA, decision curve analysis.

major procedure has not radically changed over that time. Secondly, the distribution of patients by disease severity was not well balanced. In earlier years, many patients with severe TOF did not undergo surgery. Therefore, the basic conditions of earlier patients are actually better than those of more recent patients. Additionally, improvements in surgical skills and perioperative management in recent years may be offset by disease severity. Thirdly, our hospital is the largest children's hospital in southwestern China. Primary complete repair is a mature procedure, and all the involved surgeons and nurses were experienced. We particularly emphasize that the use of the proposed model requires more external validation, especially for institutions with less surgical experience. The year of surgery and differences in the surgical team may affect the outcome and should not be completely ignored at these institutions. We hope that all doctors who perform TOF surgery have received strict training; otherwise, they may be the greatest risk factor for postoperative adverse events.

Many studies have analysed the length of hospital stay as an adverse event. However, the length of hospital stay is determined by various complications during hospitalization, and the measure itself is not the fundamental influencing factor; therefore, we did not choose length of stay as a main factor. Additionally, we did not select low cardiac output syndrome or vasopressor inotropic score as risk factors because the diagnosis of postoperative low cardiac output syndrome remains unclear; some studies in the literature refer to subjective factors (2,3,21), such as clinical symptoms, which will affect the diagnosis of low cardiac output syndrome.

There were certain limitations to our study. Firstly, it was a retrospective single-centre analysis because it was carried out in a less-developed area, which is limited by economic and technical aspects; the risk factors in this study were relatively basic indices, and tissue Doppler or postoperative magnetic resonance imaging assessments of cardiac function were not performed. Secondly, ML, which assumes sophisticated algorithms, provides references for clinical diagnosis, treatment and prediction of potential risks and requires a large sample size and external verification (22), and studies of paediatric surgery frequently cannot meet these requirements. Hence, classical algorithms such as LR should not be completely abandoned and still have good application in paediatric surgery research.

Conclusions

In summary, we found that CPB time, DP, and TP repair are risk factors for adverse events after complete repair of TOF. The risk of adverse events increases significantly when the CPB time is longer than 105 minutes or the RVOT pressure is higher than 70 mmHg. SPO_2 is a protective factor, with a reference point of 88%; the risk of adverse events increases significantly when SPO_2 is lower than 88%. ML models were established to predict the incidence of adverse events.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-246/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-246/dss

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-246/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-246/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the ethics committee of our hospital (approval number: 2021-352), and informed consent was obtained from all patients' parents or legal guardians.

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Supplementary

Table S1 Detailed parameter settings of 5 ML model

ML model	Detailed parameter settings
Logistic regression	C-index: 1, max_iter: 100, penalty: l2, tol: 0.0001
Gaussian NB	Priors: None, var_smoothing: 1e-07
Multilayer perceptron	Activation: logistic, hidden_layer_sizes: (60, 10), max_iter: 200
Support vector machine	C-index: 1.0, kernel: rbf, tol: 0.001
K-nearest neighbor	n-neighbors: 6, weights: uniform

ML, machine learning.

Table S2 Detailed feature importance by LASSO regression

Feature	Value
SPO_2	0.084
CPB-time	0.063
Gender	0.038
ACC-time	0.026
EF	0.021
Weight	0.010
PV-leaflet	0.004
Z-index	<0.001
LVEDI	≤0.001
DP	0.078
TP repair	0.057
Age	0.038
Annulus	0.024
PvO	0.013
VSD	0.007
HCT	0.002
M-index	≤0.001
Branch	≤0.001

CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; EF, ejection fraction; PV-leaflet, pulmonary valve leaflet; Z-index, pulmonary valve annulus Z score; LVEDI, left ventricular end-diastolic volume index; RVOTDP or DP, differential pressure of the right ventricular outflow tract; TP repair, transannular patch repair; PvO, opening of the pulmonary valve; VSD, ventricular septal defect; HCT, haematocrit; M-index, McGoon index.

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Table S3 Details of results in the training sets

Factors	AUC	Accuracy	Sensitivity	Specificity	Positive predictive value	Negative predictive value	F1-SCORE
LR mean	0.760	0.708	0.657	0.760	0.684	0.729	0.668
LR SD	0.010	0.012	0.038	0.048	0.036	0.019	0.008
GNB mean	0.730	0.667	0.733	0.630	0.614	0.750	0.658
GNB SD	0.012	0.023	0.113	0.117	0.058	0.048	0.030
MLP mean	0.513	0.536	0.691	0.435	0.518	0.642	0.541
MLP SD	0.069	0.064	0.302	0.336	0.081	0.115	0.106
SVM mean	0.624	0.637	0.602	0.664	0.615	0.703	0.607
SVM SD	0.155	0.032	0.305	0.179	0.074	0.065	0.124
KNN mean	0.779	0.665	0.660	0.793	0.825	0.638	0.728
KNN SD	0.035	0.009	0.068	0.022	0.067	0.002	0.034

AUC, the area under the curve; LR, logistic regression; SD, standard deviation; GNB, Gaussian Naive Bayes; MLP, multilayer perceptron; SVM, support vector machine; KNN, K-nearest neighbour.

Table S4 Details of results in the testing sets

Factors	AUC	Accuracy	Sensitivity	Specificity	Positive predictive value	Negative predictive value	F1-SCORE
LR mean	0.701	0.664	0.612	0.741	0.626	0.705	0.598
LR SD	0.062	0.033	0.180	0.134	0.124	0.055	0.105
GNB mean	0.707	0.664	0.671	0.724	0.674	0.732	0.628
GNB SD	0.012	0.022	0.204	0.202	0.173	0.114	0.044
MLP mean	0.450	0.536	0.792	0.355	0.456	0.689	0.574
MLP SD	0.065	0.040	0.199	0.215	0.034	0.073	0.083
SVM mean	0.607	0.586	0.692	0.597	0.615	0.748	0.641
SVM SD	0.180	0.066	0.368	0.219	0.117	0.164	0.153
KNN mean	0.523	0.545	0.314	0.795	0.523	0.549	0.352
KNN SD	0.139	0.020	0.341	0.262	0.125	0.040	0.114

AUC, the area under the curve; LR, logistic regression; SD, standard deviation; GNB, Gaussian Naive Bayes; MLP, multilayer perceptron; SVM, support vector machine; KNN, K-nearest neighbour.

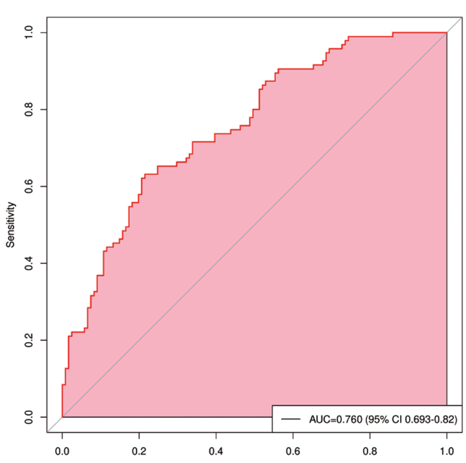

Figure S1 AUC of the LR model. AUC, the area under the curve; CI, confidence interval; LR, logistic regression.

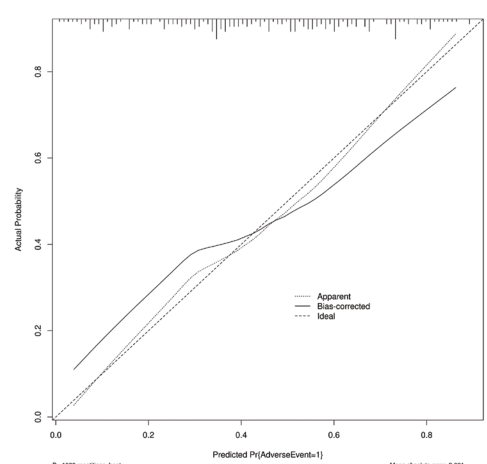

Figure S2 Expected and observed probability of adverse events by the Hosmer-Lemeshow test.

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