

Frequency of Postoperative Fever in Children with Congenital Heart Disease Undergoing Cardiovascular Surgery and Associated Risk Factors

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Objectives. To determine the frequency of postoperative fever in children with congenital heart disease who undergo cardiovascular surgery, and the risk factors associated.

Patients and methods. In a prospective cohort study, 100 children under the age of less than 9 years were followed-up during hospitalization in order to detect fever after cardiac surgery. Preoperative, perioperative, and postoperative variables were assessed to determine their relationship with postoperative fever. The cases were patients who developed fever. Multivariate analysis was used, and the odds ratio (OR) and 95% confidence intervals (95% CI) were calculated.

Results. The frequency of postoperative fever was 46%. Fever appeared within 24 hours of surgery in 56% cases. In 32/46 (70%) cases, fever remitted within 72 hours. Fever was more common in patients who underwent open-heart surgery than in those treated with a closed technique (28 vs. 18, $P = 0.045$). Prolonged extracorporeal circulation (OR = 1.024; 95% CI, 1.004-1.045), aortic cross-clamping (OR = 2.83; 95% CI, 1.21-6.61) and postoperative infections (OR = 24.07; 95% CI, 7.2-75.0) were the risk factors associated with the development of postoperative fever.

Conclusions. Postoperative fever is common in children with congenital heart disease. The identification of risk factors associated to the development of fever should help clinicians to identify the cause of fever in this group of patients.

Key words: *Pediatrics. Congenital heart disease. Surgery. Postoperative complications. Fever.*

Frecuencia y factores de riesgo asociados con el desarrollo de fiebre postoperatoria en niños con cardiopatía congénita sometidos a cirugía cardiovascular

Objetivos. Determinar la frecuencia y los factores de riesgo asociados al desarrollo de fiebre postoperatoria en niños con cardiopatía congénita sometidos a cirugía cardiovascular.

Pacientes y métodos. Estudio de una cohorte prospectiva. Cien niños menores de nueve años sometidos a cirugía cardiovascular fueron vigilados durante su estancia hospitalaria para identificar la presencia de fiebre después de la cirugía. Se registraron variables pre, trans y postoperatorias para determinar su asociación con fiebre. Los casos fueron pacientes que desarrollaron fiebre. Se realizó análisis multivariado, calculándose *odds ratio* e intervalos de confianza del 95% (IC del 95%).

Resultados. La frecuencia de fiebre postoperatoria fue del 46%; en el 56% de los casos la fiebre ocurrió dentro de las primeras 24 horas después de la cirugía, y en 32/46 (70%) casos la fiebre se resolvió en menos de 72 horas. La frecuencia de fiebre fue mayor en pacientes sometidos a cirugía intracardiaca que en cirugía extracardiaca (28 frente a 18, $p = 0.045$). Los factores de riesgo asociados a fiebre postoperatoria fueron: mayor tiempo de bomba de circulación extracorpórea (OR = 1.024; IC del 95%, 1.004-1.045), pinzamiento aórtico (OR = 2.83; IC del 95%, 1.21-6.61) e infecciones en el período postoperatorio (OR = 24.07; IC del 95%, 7.2-75.0).

Conclusiones. El desarrollo de fiebre postoperatoria en niños con cardiopatía congénita es un acontecimiento frecuente. Los factores de riesgo encontrados en este estudio pueden ayudar a los clínicos para orientarlos en la búsqueda de la causa de fiebre en estos pacientes.

Palabras clave: *Pediatría. Cardiopatías congénitas. Cirugía. Complicaciones postoperatorias. Fiebre.*

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INTRODUCTION

The elevation of body temperature after a surgical procedure is known as postoperative fever.^{1,2} The frequency of postoperative fever differs depending on the type of surgery: in orthopedics it ranges from 39% to 100%; in gynecology it is approxima-

ABBREVIATIONS

ASD: atrial septal defect
VSD: ventricular septal defect
PDA: persistent ductus arteriosus
OR: odds ratio
CI: confidence interval

tely 40%, and in abdominal surgery it is less than 10%.³⁻⁵

Information about the frequency of postoperative fever in cardiovascular surgery is limited, and the figures cited vary. To date, frequencies of 12% to 73%⁶⁻⁸ have been described in studies of adult patients⁶ or of adults and children.⁸ Only the study by Bell et al,⁷ out of all these studies, specified that the type of surgery performed was valvular. There does not seem to be any consensus regarding the time of onset of fever, with some authors reporting that it appears in the first 48 h after surgery,⁸ and others on day 6 of the postoperative period.⁶

Other studies have investigated the causes related to the onset and duration of postoperative fever. In general, the presence of fever is considered to be associated with the metabolic response to trauma, duration of surgery, the accumulation of blood in closed spaces, use of drainage tubes, drugs administered during the perioperative period, and infections.^{2-4,9} Some authors consider that the inflammatory response secondary to surgery is the main factor associated with postoperative fever.¹⁰⁻¹² In cardiovascular surgery, this type of fever has generally been related with the use of an extracorporeal circulation pump during cardiopulmonary bypass, hypothermia, and the post-perfusion syndrome,¹²⁻¹⁵ as well as infections, blood transfusions, dehydration, and atelectasis.^{1,6-8,16,17}

In view of the fact that the information on postoperative fever in patients undergoing cardiovascular surgery is mainly from studies in adults, the objectives of the present study were: *a)* to estimate the frequency of postoperative fever in children with congenital heart disease undergoing cardiovascular surgery, and *b)* to identify the risk factors associated with the development of postoperative fever in this group of patients.

PATIENTS AND METHODS

This is a case-control study within the context of a prospective cohort study carried out between 1 January 1997 and 31 December 1998 at the Pediatrics and Cardiology Hospitals of Centro Médico Nacional Siglo XXI, Mexican Institute of Social Security, Mexico City. These hospitals are tertiary reference centers that receive referrals from the general hospitals of at least five states of the Mexican Republic. The

protocol was approved by the investigational review boards and ethics committees of both hospitals.

Patients

The study included children under the age of 9 years with a diagnosis of congenital heart disease who were scheduled to undergo cardiovascular surgery for the first time. For admission to the study, patients had to be free of fever or any infectious process prior to surgery; patients who died in the perioperative period or in the first 24 h after surgery without fever were excluded.

Monitoring

The children who met the selection criteria were followed-up from the time of admission to the hospital to the day of intervention and afterward. Follow-up was daily in the intensive care unit and hospital ward, and concluded at the time of hospital discharge.

Two of the authors collected information about every variable from the clinical dossier (medical history, postoperative and anesthesia records) and from the nursing records using special forms. Before beginning the study, the forms and evaluators were standardized.

Variables

The information was divided into three groups: preoperative, perioperative, and postoperative variables. The preoperative information included: age, sex, nutritional state, type of congenital heart disease, presence of pulmonary hypertension, fever, rhinorrhea or cough, and duration of the preoperative hospital stay. Perioperative variables: type of surgery (intracardiac or extracardiac), type of anesthesia, drugs administered (antibiotics, anesthetics), and use of hypothermia. The duration of the intervention and, when applicable, the use of cardiopulmonary bypass and aortic clamping, were recorded. Postoperative variables: presence of fever, day of onset, duration, and infectious complications. The condition of the patient at the time of hospital discharge and the total duration of the hospital stay were recorded.

Definitions

Cases were patients who presented fever at any time after surgery. *Controls* were patients who did not present fever during the monitoring period from the end of surgery to the time of hospital discharge.

Fever was defined as an axillary temperature of $\geq 38^{\circ}\text{C}$ recorded at any time after surgery, in two or more instances during a 24-h period. This information was obtained from nursing records.

Statistical analysis

A sample size of 100 patients was estimated after taking into consideration a frequency of fever of 25% and a 95% confidence interval (CI) of 13% to 29%, and alpha 0.05. The sample size for the study of the association of independent variables and the presence of fever was calculated considering a logistical regression analysis,¹⁸ alpha level of 0.05, beta level of 0.10, and a difference in the exposure factor of 50%, resulting in $n=104$.

The results of the descriptive analysis of quantitative variables was expressed as medians and minimum and maximum values because the distribution was not normal. Quantitative variables were compared between cases and controls using the Mann-Whitney U test; qualitative variables were compared using the χ^2 or Fischer exact test. A value of $P<.05$ was considered significant. The multivariate analysis used to determine the association of fever with preoperative, perioperative, and postoperative variables was conditional inverse logistic regression; the odds ratio and 95% CI were calculated. The variables in which univariate analysis yielded $P\geq.25$ were admitted to the models. Analyses were made with the SPSS v.10.0 statistical package (SPSS Inc., Chicago, Illinois).

RESULTS

One hundred patients with an age range of 1 day to 8 years and a month were included; the median age was 17.5 months and 67% were females. The most frequent heart diseases were persistent ductus arteriosus (PDA), atrial septal defect (ASD), and ventricular septal defect (VSD). Extracardiac surgery was performed in 50 patients. The most frequent surgical procedures were ligation of PDA (26 cases; 52%) and resection of an aortic coarctation (11 cases; 22%). Of the intracardiac procedures, VSD closure, alone or in combination with correction of PDA or ASD, was the most frequent intervention (17 cases; 34%), followed by ASD closure (15 cases; 30%). All patients received balanced general anesthesia with fentanyl (97%), vecuronium (87%), isoflurane (83%) and/or propofol (70%).

Frequency of fever

There were 46 episodes of fever in 46 patients at some moment after the intervention (46%). The onset of fever occurred at a median of one day. Fever appeared in 26 cases (56%) in the first hours after surgery, in 35 patients in the first 48 h, and in one patient (2%) on postoperative day 10. Of the 26 patients who had fever the first day, it appeared in the first 12 h of the postoperative period in 24 patients and in the first 2 h in 2 patients.

The median duration of fever was 2 days; in approximately 70% (32/46) of the patients the fever resolved within 72 h of onset. The fever persisted 11 days in only 1 patient. The duration of fever differed according to the day of onset. When the episodes began in the first 48 h after surgery, the median duration was 2 days (minimum 1 day and maximum 11 days). In the other 11, the median duration was 3 days (minimum 1 day and maximum 7 days), although the difference was not significant ($P=.7$).

The frequency of fever in relation to the main diagnosis and type of surgery is shown in Table 1. Fever was more frequent ($P=.045$) in the intracardiac surgery group (28 episodes; 56%) than in the extracardiac surgery group (18 episodes; 36%). Whereas the median onset (1 day in both groups) and duration of fever (2.5 versus 2 days) were similar; 16/26 patients whose fever began in the first 24 h had undergone intracardiac surgery. In the extracardiac surgery group, resection of an aortic coarctation and cavopulmonary bypass were the procedures in which fever appeared most frequently. In the intracardiac surgery group, the correction of more than one defect (ASD+VSD, tetralogy of Fallot, etc.) were the procedures most frequently accompanied by fever.

Comparison of cases and controls

In Tables 2-4, the preoperative, perioperative, and postoperative variables are compared in the patients

TABLE 1. Frequency of fever by type of surgery and main diagnosis

Type of surgery	Main diagnosis	Frequency of fever (n=46)		
		No.		Percentage
Intracardiac (n=50)	ASD	8	3	37.5
	VSD	7	3	42.9
	APVD	7	2	28.6
	ASD+PDA	7	2	28.6
	VSD+PDA	7	6	85.7
	Tetralogy of Fallot	4	4	100
	AV canal	4	3	75
	ASD+VSD	3	3	100
	TGA	2	1	50
	RV hypoplasia	1	1	100
Extracardiac (n=50)	PDA	26	5	19.2
	Coarctation of the aorta	11	5	45.5
	Pulmonary atresia	9	6	66.7
	DRVOT	2	1	50
	Aberrant right subclavian	1	1	100
	Subaortic stenosis	1	0	—

ASD indicates atrial septal defect; VSD, ventricular septal defect; AV, atrioventricular; APVD, anomalous pulmonary venous drainage; DRVOT, double right ventricular outflow tract; PDA, persistent ductus arteriosus; TGA, transposition of great arteries; RV, right ventricle.

TABLE 2. Comparison of the preoperative characteristics of patients who developed fever (cases) and those who did not (controls)

Characteristic	Cases, n=46	Controls, n=54	P
Age, months	16 (0-97) *	21.5 (0-79)	.22
Sex			
Male	17 (37)	16 (30)	.52
Female	29 (63)	38 (70)	
Main diagnosis of type of heart disease	5 (11)	21 (39)	
PDA	5 (11)	6 (11)	
Coarctation of the aorta	6 (13)	3 (5)	
Pulmonary atresia	3 (6)	5 (9)	.02
ASD	6 (13)	1 (2)	
VSD+PDA	3 (6)	4 (7)	
VSD	2 (4)	5 (9)	
ASD+PDA	2 (4)	5 (9)	
APVD	4 (9)	0	
of Fallot	3 (6)	0	
ASD+VSD	3 (6)	1 (2)	
Atrioventricular canal	1 (2)	1 (2)	
TGA	1 (2)	1 (2)	
DRVOT	2 (4)	1 (2)	
Others**			
Nutritional status			
Normal	15 (33)	24 (45)	.51
First-degree nutritional deficiency	9 (20)	12 (22)	
Second-degree nutritional deficiency	16 (35)	13 (24)	
Third-degree nutritional deficiency	6 (13)	5 (9)	
Days of hospitalization before surgery	2 (1-18)	3 (1-14)	.20

ASD indicates atrial septal defect; VSD, ventricular septal defect; APVD, anomalous pulmonary venous drainage; DRVOT, double right ventricular outflow tract; PDA, persistent ductus arteriosus; TGA, transposition of great arteries.

*Quantitative values are shown as medians, with the minimum and maximum values in parentheses. Qualitative values are shown as whole numbers, with percentages in parentheses.

**Right ventricular hypoplasia (1), subaortic stenosis (1), aberrant right subclavian (1).

who presented fever (cases) and in those who did not (controls). In Table 2 it is observed that, with the exception of the type of heart disease, there were no differences in the variables considered in the preoperative period. By type of heart disease, there was a greater proportion of children with PDA alone ($P=.003$), or PDA in combination with VSD or ASD, in controls. Patients with tetralogy of Fallot ($P=.09$) or VSD with ASD ($P=.19$) were observed only in the group of cases.

In relation to the perioperative variables (Table 3), the cases had higher percentages of intracardiac surgery, aortic clamping, use of cardiopulmonary bypass, and hypothermia ($P<.05$). In the intracardiac surgery group, the duration of surgery was also significantly

TABLE 3. Perioperative characteristics of the children included and comparison of the patients who developed fever (cases) and those who did not (controls)

Characteristic	Cases, n=46	Controls, n=54	P
Type of surgery			
Extracardiac	18 (39)	32 (59)	.045
Intracardiac	28 (61)	22 (41)	
Duration of intervention, min	212.5 (80-300)	155 (75-360)	.008
Aortic clamping	34 (74)	27 (50)	.015
Clamping time, min	40.5 (2-120)	29 (7-69)	.091
Cardiopulmonary bypass	33 (72)	26 (48)	.017
Cardiopulmonary bypass time, min	79 (25-217)	65 (19-150)	.093
Hypothermia	29 (63)	23 (33)	.041
Type of incision			
Medial	30 (65)	27 (50)	.15
Lateral	16 (35)	26 (48)	

*Quantitative values are shown as medians, with the minimum and maximum values in parentheses. Qualitative values are shown as whole numbers, with percentages in parentheses.

more prolonged than in controls. Although the duration of clamping and cardiopulmonary bypass were greater in cases, the difference was not statistically significant.

Of the postoperative variables (Table 4), there was a significantly greater proportion of infectious and non-infectious complications in cases. The most frequent infectious processes were pneumonia and phlebitis. Among the non-infectious complications, the most frequent were metabolic acidosis, acute kidney failure, and seizures.

On the other hand, the patients who presented fever had significantly longer stays in both the hospital and intensive care unit. During monitoring, 5 patients died, 4 cases and 1 control; the difference was not significant.

Factors associated with postoperative fever in multivariate analysis

The first models were developed with variables from every period; the only significant preoperative variable was the diagnosis of PDA (odds ratio [OR]: 0.28; 95% CI, 0.09-0.86). Significant perioperative variables were aortic clamping (OR, 2.83, 95% CI, 1.21-6.61) and, after controlling for aortic clamping, use of cardiopulmonary bypass, or intracardiac surgery, the longer duration of cardiopulmonary bypass (OR, 1.024; 95% CI, 1.004-1.045). In patients with extracardiac surgery, a more prolonged duration of surgery was associated with fever (OR, 1.015; 95% CI, 1.015-1.028). The variables of the postoperative period associated with fever were the presence of infection (OR, 24.0; 95% CI, 7.27-75.0) and postoperative complica-

TABLE 4. Postoperative characteristics of the children included and comparison of the patients who developed fever (cases) and those who did not (controls)

Characteristic	Cases,* n=46	Controls,** n=54	P
Number of patients			
with infection	26 (56)	5 (9)	<.0001
Site of infection**			
Pneumonia	19 (41)	3 (6)	
Urinary tract	2 (4)	1 (2)	
Surgical wound	2 (4)	1 (2)	
Acute otitis media	1 (2)	0	
Sinusitis	2 (4)	0	<.0001
Phlebitis	6 (13)	0	
Sepsis	4 (9)	1 (2)	
Empyema	1 (2)	1 (2)	
Number of patients with one or more complications	17 (37)	3 (6)	<.0001
Complications**			
Metabolic acidosis	5 (11)	0	
Acute kidney failure	5 (11)	0	
Seizures	4 (9)	0	
Pleural effusion	2 (4)	0	<.001
Cardiorespiratory arrest	1 (2)	1 (2)	
Acute lung edema	0	1 (2)	
Pneumothorax	0	1 (2)	
Others***	7 (15)	0	
Death	4 (9)	1 (2)	.17
Days of intensive care stay	6 (1-24)	4 (1-24)	.002
Total hospital stay, days	13 (3-43)	9 (1-26)	.001

*Quantitative values are shown as medians, with the minimum and maximum values in parentheses. Qualitative values are shown as whole numbers, with percentages in parentheses.

**One or more characteristics may correspond to a patient.

***Atrioventricular block, cardiogenic shock, hemorrhagic cystitis, heart failure, supraventricular tachycardia, thrombosis of the longitudinal sinus, duodenal ulcer.

tions (OR, 10.3; 95% CI, 2.1-50.8). The significant variables of the three periods were analyzed together, the postoperative variables remained independent (OR, 12.5; 95% CI, 3.1-50.2, and OR, 11.5; 95% CI, 1.8-70.2, respectively). When these variables were not considered, only the diagnosis of PDA was significant (OR, 0.19; 95% CI, 0.065-0.53). However, when the type of surgery was controlled this variable ceased to be significant. In the group of intracardiac surgery, the duration of cardiopulmonary bypass had an OR of 1.015 and 95% CI, 0.99-1.032.

DISCUSSION

Postoperative fever has been the topic of study in several publications, but information on this phenomenon in children is scant, particularly in cardiovascular surgery. In recent years research on this subject has focused on the immunological aspects of the physiology

of its pathogenesis^{12,19-21} and on the evaluation of treatments to reduce its incidence.²²

The results of the present study provide more information on the frequency and characteristics of postoperative fever in children with congenital heart disease undergoing cardiovascular surgery. The frequency of this phenomenon was 46%, but when frequency was analyzed by type of intervention, it was 56% in patients undergoing intracardiac surgery and 38% in patients undergoing extracardiac surgery. These results are very different from those reported in the only publication describing this phenomenon in children.⁸ In that study, fever was more frequent overall and it is noteworthy that all the patients who underwent surgery with cardiopulmonary bypass presented fever. Nevertheless, the frequency of fever was higher in children over the age of five years, in contrast with the findings of our study. In comparison with reports of adults undergoing cardiovascular surgery, in which the frequency of fever is about 30%,^{6,7} fever was more frequent in this study. These findings, together with those of Andrade et al,⁸ suggest the hypothesis that the frequency of postoperative fever in children could be greater than in adults.

This study disclosed findings that have not been described previously. The study design included patient monitoring throughout the postoperative period until hospital discharge. This made it possible to determine that fever most frequently appeared in the immediate postoperative period. In patients who suffered fever of earlier onset, it resolved within 72 h, but this finding was not statistically significant.

One of the reasons for carrying out this study was that clinicians responsible for caring for children in the postoperative period of cardiovascular surgery find it difficult to determine the cause of fever.¹⁷ Generally, the presence of fever indicates the possibility of infection, which leads to a search for the focus or, due to its severity, to the early empirical use of antimicrobial agents. Although the use of antimicrobial agents may be justified, there are patients who do not benefit from this practice. Consequently, we have sought factors that can help clinicians to differentiate between cases of fever due to infection and those due to other causes. The variables investigated were those that have generally been identified as causes of fever in any type of surgery, in addition to procedures used in cardiovascular surgery.

Univariate analysis disclosed differences between the patients who developed fever in the preoperative and perioperative period and those who did not. Only one preoperative variable was related with postoperative fever: patients who underwent repair of PDA alone had less probability of developing fever. On the other hand, almost all the perioperative variables studied were associated with fever, particularly a more prolonged duration of surgery and the use of aortic

clamping, cardiopulmonary bypass, and hypothermia.

The perioperative factors that reached statistical significance were analyzed in different multivariate analysis models to determine their true influence on the development of postoperative fever. The results demonstrated that more prolonged cardiopulmonary bypass time and aortic clamping (but not the duration of aortic clamping) were the variables associated more frequently with fever. Since these procedures were not performed in all the patients who underwent cardiovascular surgery, two more models were examined: patients who underwent intracardiac surgery and patients who underwent extracardiac surgery. Fever was associated with more prolonged cardiopulmonary bypass in patients who underwent intracardiac surgery, and with a longer duration of surgery in the patients who underwent extracardiac surgery. It should be noted that the diagnosis of PDA was considered a protective factor or an indicator of a lower probability of developing fever in the model that included all the variables. This was attributed to the fact that this type of heart disease (Table 1) was the most frequent and was accompanied by the frequency of fever (19%). In general, correction of this type of heart disease involves technically simpler procedures; in this group, the median duration of the operation was shorter (125 min) than in the rest of the heart diseases.

In general, the risk factors identified seemed to share a common pathophysiology for the development of fever: activation of the immune response.¹⁰⁻¹² Various studies have shown that interleukins are released after cardiopulmonary bypass, aortic clamping, and hypothermia in cardiovascular surgery.^{12,14,20} The same mechanism seems to be involved whenever the duration of surgery is extended. Considering that the immune response is the main cause of fever, various authors have tried to curtail the inflammatory response with steroids in the preoperative and perioperative period.^{23,24} The results are still controversial and it has not yet been possible to determine the advantages of using them to reduce the incidence of postoperative fever.^{22,25-27} In Mexico, where the present study was made, steroids are not used systematically.

It should not be forgotten that infectious processes play an important role in the development of postoperative fever.¹ In the analysis of risk factors, the presence of some sort of infection in the postoperative period was the most important variable. However, some observations should be made. The study design did not establish any methods to follow. Consequently, patients with some type of infection were identified in accordance with the treating physician's criterion and the medical record. It can be argued that in the presence of fever, physicians tend to overdiagnose infections when clinical findings are not insufficient for the diagnosis of an infectious process. We examined this pos-

sibility with the cases of pneumonia, the infection most often documented, in an independent analysis. From the start it was noteworthy that were patients diagnosed as pneumonia that did not have fever. In addition, in 14/19 (74%) patients with fever, the fever began in the first 48 h of the postoperative period. Normally, if the clinical condition of the patients allows, one of the criteria for cardiovascular surgery is the absence of any infectious process. From the moment in which the study was planned, only patients free of infectious processes and with no clinical manifestations of infection (cough, rhinorrhea, etc.) were selected. This lead us to question whether or not these patients actually had pneumonia, particularly in 8 of the 14 patients (57%) with early onset fever that resolved within 48 h. In view of these findings and the other risk factors identified in the perioperative period, we propose that physicians examine the full range of possible causes of fever when confronted with patients like those included in this study.

In conclusion, postoperative fever seems to be frequent in children with congenital heart disease undergoing cardiovascular surgery, particularly when intracardiac surgery is performed. Perioperative factors associated with fever, such as a longer duration of surgery, use of cardiopulmonary bypass, and aortic clamping, have a common immunological pathophysiology. We hope that these results motivate physicians to broaden their views to include other possibilities in addition to infection when fever appears in the postoperative period, particularly in the immediate postoperative period.

REFERENCES

1. Lenhardt R, Negishi C, Sessler DI. Perioperative fever. *Acta Anaesthesiol Scand Suppl* 1997;111:325-8.
2. Frank SM, Kluger MJ, Kunkel SL. Elevated thermodynamic setpoint in postoperative patients. *Anesthesiology* 2000;93:1426-31.
3. Than P, Malovics I. Significance of postoperative fever after hip prosthesis implantation. *Z Orthop Ihre Grenzgeb* 2000;138:430-5.
4. Fanning J, Neuhoft RA, Brewer JE, Castaneda T, Marcotte MP, Jacobson RL. Frequency and yield of postoperative fever evaluation. *Infect Dis Obstet Gynecol* 1998;6:252-5.
5. Riesener KP, Lehnen W, Hofer M, Kasperk R, Braun JC, Shumpelick V. Morbidity of ileostomy and colostomy closure: impact of surgical technique and perioperative treatment. *World J Surg* 1997;21:103-8.
6. Livelli FD Jr, Johnson RA, McEnany MT, Sherman E, Newell J, Block PC, et al. Unexplained in-hospital fever following cardiac surgery. Natural history, relationship to postpericardiotomy syndrome, and a prospective study of therapy with indomethacin versus placebo. *Circulation* 1978;57:968-75.
7. Bell DM, Goldmann DA, Hopkins CC, Karchmer AW, Moellering RC Jr. Unreliability of fever and leukocytosis in the diagnosis of infection after cardiac valve surgery. *J Thorac Cardiovasc Surg* 1978;75:87-90.

8. Andrade CL, Olvera S, Reyes PA. Fiebre e infección después de cirugía cardíaca. Estudio prospectivo en 75 casos. *Arch Inst Cardiol Mex* 1989;59:487-91.
9. Knowles SR, Vetter J, Shear NH. Idiosyncratic drug reactions: the reactive metabolites syndromes. *Lancet* 2000;356:1587-91.
10. Reber PU, Sanderg A, Schmied B, Buchler MW. Cytokines in surgical trauma: cholecistectomy as an example. *Dig Surg* 1998;15:92-101.
11. Jess P, Schultz K, Bendtzen K, Nielsen OH. Systemic inflammatory responses during laparoscopic and open inguinal hernia repair: a randomised prospective study. *Eur J Surg* 2000;166:540-4.
12. Carvalho MV, Maluf MA, Catani R, La Rotta CA, Gomes WJ, Salamao R, et al. Cytokines and pediatric open heart surgery with cardiopulmonary bypass. *Cardiol Young* 2001;11:36-43.
13. Bert AA. Systemic effects of normothermic cardiopulmonary bypass. *Artif Organs* 1998;22:77-81.
14. Cremer J, Martin M, Redl H, Bahrami S, Abraham C, Graeter T, et al. Systemic inflammatory response after cardiopulmonary bypass. *Ann Thorac Surg* 1996;61:1714-20.
15. Seghaye MC, Grabitz RG, Duchateau J, Busse S, Dabritz S, Koch D, et al. Inflammatory reaction and capillary leak syndrome related to cardiopulmonary bypass in neonates undergoing cardiac operations. *J Thorac Cardiovasc Surg* 1996;112:687-97.
16. Verkkala K, Valtonen V, Jarvinen A, Tolppanen EM. Fever, leucocytosis and C-reactive protein after open-heart surgery and their value in the diagnosis of postoperative infections. *Thorac Cardiovasc Surg* 1987;35:78-82.
17. Aouiffi A, Piriou V, Bastein O, Blanc P, Bouvier H, Evans R, et al. Usefulness of prolactinin for diagnosis of infection in cardiac surgical patients. *Crit Care Med* 2000;28:3171-6.
18. Agresti A. Logistic regression. En: Agresti A, editor. *An introduction to categorical data analysis*. New York: John Wiley & Sons, 1996; p. 103-44.
19. Duval EI, Kavelaars A, Veenhuizen L, Van Vught AJ, Van de Wal HJ, Heijnen CJ. Pro- and anti-inflammatory cytokine patterns during and after cardiac surgery in young children. *Eur J Pediatr* 1999;158:387-93.
20. Mitchell IM, Brady L, Black J, Jamieson MP, Pollock JC, Logan RW. The acute phase response to cardiopulmonary bypass in children. *Perfusion* 1996;11:103-12.
21. Sugita T, Watarida S, Katsuyama K, Nakajima Y, Yamamoto R, Mori A. Interleukin-10 concentration in children undergoing cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1996;112:1127-8.
22. Butler J, Pathi V, Paton RD, Paton RD, Logan RW, MacArthur KJ, et al. Acute-phase responses to cardiopulmonary bypass in children weighing less than 10 kilograms. *Ann Thorac Surg* 1996;62:538-42.
23. Yared JP, Starr NJ, Torres FK, Bashour CA, Bourdakos G, Piedmonte M, et al. Effects of single dose, postinduction dexamethasone on recovery after cardiac surgery. *Ann Thorac Surg* 2000;69:1420-4.
24. Nagelschmidt M, Fu ZX, Saad S, Dimmeler S, Neugebauer E. Preoperative high dose methylprednisolone improves patients outcome after abdominal surgery. *Eur J Surg* 1999;165:971-8.
25. Sauerland S, Nagelschmidt M, Mallmann P, Neugebauer EA. Risks and benefits of preoperative high dose methylprednisolone in surgical patients: a systematic review. *Drug Saf* 2000;23:449-61.
26. Mott AR, Fraser CD Jr, Kusnoor AV, Giesecke NM, Reul GJ Jr, Drescher KL, et al. The effect of short-term prophylactic methylprednisolone on the incidence and severity of postpericardiotomy syndrome in children undergoing cardiac surgery with cardiopulmonary bypass. *J Am Coll Cardiol* 2001;37:1700-6.
27. Yared JP, Starr NJ, Hoffmann-Hogg L, Bashour CA, Insler SR, O'Connor M, et al. Dexamethasone decreases the incidence of shivering after cardiac surgery: a randomized, double-blind, placebo-controlled study. *Anesth Analg* 1998;87:795-9.