

Children with post-rheumatic valvulopathies in natural history: five years follow-up in the Cardiac Centre, St. Elizabeth Catholic General Hospital Shisong (Cameroon)

Enfants porteurs de valvulopathies post rhumatismales en « histoire naturelle » : suivi de 5 ans au Centre cardiaque de l'hôpital de Shisong (Cameroun)

J.C. Tantchou Tchoumi · J.C. Ambassa · G. Butera

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Abstract The aim of the study was to investigate the pattern of valvular lesions, the mortality and the challenges in five years follow-up in children with post-rheumatic valvulopathies in natural history in St. Elizabeth Catholic General hospital Shisong, cardiac centre. This retrospective analysis included 270 patients aged between 5 and 16 years old suffering from post-rheumatic valvulopathies who consulted in the cardiac centre from July 2008 through July 2013. Post-rheumatic valvulopathies were diagnosed according to the World heart federation criteria. Data from patients' records, two-dimensional echocardiographic studies, and electrocardiograms were reviewed. Patients and their family were contacted every six months. The duration of the follow-up was 60 months. Patients aged between 5 and 16 years old with a mean age of 12.4±4.5 years. Female gender was representing 63% (n=170) of the population. Surgery was indicated in 256 cases. Lesions of the valves needing prophylaxis with penicillin was diagnosed in 14 cases. In 95 patients surgical correction could not be performed. Mitral regurgitation was the commonest echocardiographic diagnosis present in 61.5%, n=164 patients; 38.5%, n=103 patients had aortic regurgitation. Mitral stenosis and mitral disease were also represented in 6%, n=16, and 8%, n= 21 patients respectively. Pulmonary hypertension was the common echocardiographic complication of the disease in=234, 87% of cases. Clinically, complications of the disease included congestive heart failure (n=229, 85%), growth retardation (n=162, 60%), sudden

death (n=27, 10%). On presentation, n=210, 78% of cases were admitted. Mortality in two years was 35%, (p≤0.05, 95% CI=2.5 – 6.5), in five years was 65% (p≤ 0.05, 93% CI= 2.7 – 7.21). The challenges faced are patients' negligence and poor discipline, wrong beliefs, poverty. Post-rheumatic mitral valve regurgitation is the pathology the most encountered. Pulmonary hypertension is the most common echocardiographic complication of the disease. Five years mortality is very high in our setting. Due to financial limitation and illiteracy of parents, the follow up of patients is difficult.

Keywords Post-rheumatic valvulopathy · Children · Mortality · Hospital · Shisong · Cameroon · Sub-Saharan Africa

Résumé L'objectif de l'étude était d'observer sur cinq ans l'évolution des lésions valvulaires, la mortalité et les défis sur des enfants porteurs de valvulopathies post rhumatismales en « histoire naturelle » au Centre cardiaque du Ste. Elizabeth Catholic General hospital de Shisong. 270 patients âgés de 5 à 16 ans, souffrant de valvulopathies post-rhumatismales et ayant consulté au Centre cardiaque de Shisong de juillet 2008 à juillet 2013 ont été inclus dans cette analyse rétrospective. Les valvulopathies post-rhumatismales étaient diagnostiquées en utilisant les critères de la Fédération mondiale du cœur. Les données des fichiers des malades, des études échocardiographiques bidimensionnelles et des électrocardiogrammes ont été consultées. Les malades et leurs familles étaient contactés bi-annuellement. La durée du suivi était de 60 mois. L'âge moyen des patients était de 12,4±4,5 ans. Le sexe féminin représentait 63 % des cas (n = 230). La chirurgie était indiquée dans 94 % des cas (n = 256). Les lésions valvulaires nécessitant une prophylaxie par pénicilline concernaient 14 personnes. La correction chirurgicale des valvulopathies n'a pas pu être effectuée chez 95 enfants. L'insuffisance mitrale était le diagnostic échocardiographique le plus

J.C. Tantchou Tchoumi (✉) · J.C. Ambassa
Centre cardiaque de l'hôpital catholique Sainte Elisabeth
de Shisong, P.O. Box 8 Kumbo, Cameroun
e-mail : tantchouj@yahoo.fr

G. Butera
Departement de chirurgie cardiaque,
Istituto Policlinico San Donato, IRCCS Via Morandi 30,
20097 San Donato Milanese, Milan, Italie

commun, présent chez 61,5 % des patients (n = 164) ; 38,5 % (n = 103) avaient une insuffisance aortique, 6 % (n = 16) une sténose mitrale, 8 % (n = 21) une maladie mitrale L'hypertension pulmonaire était la complication la plus commune de la maladie, trouvée chez 87 % des patients (n = 234). Cliniquement, les complications de la maladie incluaient l'insuffisance cardiaque congestive, dans 85 % des cas (n = 229), le retard de croissance (n = 162, 60 %), la mort subite (n = 27, 10 %). À la première présentation, 78 % (n = 210) des malades étaient hospitalisés. La mortalité après deux ans était de 35 % ($p \leq 0,05$, 95 % CI = 2,5 – 6,5), et après cinq ans de 65 % ($p \leq 0,05$, 93 % CI = 2,7 – 7,21). Les défis rencontrés sont : la négligence de la part des malades, l'absence de discipline, les croyances, la pauvreté. Dans notre étude, l'insuffisance mitrale postrhumatisme est la pathologie prévalente et l'hypertension pulmonaire, la complication échocardiographique la plus commune. La mortalité après cinq ans est très élevée dans notre contexte. La situation financière précaire et le manque d'éducation des parents rendent le suivi bien difficile.

Mots clés Valvulopathie post rhumatismale · Enfants · Mortalité · Hôpital · Shisong · Cameroun · Afrique intertropicale

Introduction

Rheumatic Heart Disease (RHD) is the most important sequelae of acute rheumatic fever, which is caused by group A streptococci and usually presents in childhood, affecting 5 to 14 years old although it can strike people up to the age of 30 [2,14]. In poor and developing nations, it remains a major cause of morbidity and premature death, imposing a substantial burden on healthcare systems with limited budgets [3,25].

The incidence of RHD in the world is at least 15.6 million cases; the highest documented prevalence of the disease among children from developing countries in sub-Saharan Africa is 5.7 per 1.000 [4,6]. The main valves severely damaged by endocarditis are the mitral and the aortic valves. The aim of the study was to investigate the pattern of valvular lesions, the mortality and the challenges in five years follow-up in children with post-rheumatic valvulopathies in natural history in St. Elizabeth Catholic General hospital, cardiac centre.

Material and methods

Patients

The study was approved by the Ethics Committee of the St. Elizabeth catholic general hospital, Shisong. In the study

were recruited 270 children with post-rheumatic valvulopathies at various stages. A total of 470 children were recruited over this period: 170 with congenital pathologies, 30 in good health and 270 included in the study. Post-rheumatic valvulopathies were diagnosed according to the World heart federation criteria [18]. Transthoracic echocardiography was performed using commercially available echocardiography equipment (Acuson Sequoia, Acuson Co, Mountain View USA) with a 3.5MHz transducer. Left ventricular systolic performance was assessed by determination of the ejection fraction, the left ventricular systolic and diastolic volumes. The regurgitation was quantified using the Proximal Isovelocity Proximal area (PISA) and the following parameters were calculated: effective regurgitant orifice area, mitral regurgitant volume [11,15]. Mitral and aortic stenosis were evaluated using the mean gradient through the valves, the valves area, and the velocity across the valve [17]. Vena contracta was measured where possible. The right atrioventricular valve was assessed for regurgitation and the right ventricular pressure estimated from the Doppler signal when possible, the tricuspid annular plane systolic excursion (TAPSE) was also measured [1,7]. Patients were reviewed every three months in the cardiac centre Shisong in a duration of 60 months. Data from patients' records, patient's outpatient department booklet electrocardiographic, two-dimensional echocardiographic studies were reviewed.

Statistical analysis

Statistical analyses were performed using the X^2 test and the Wilcoxon rank sum test for non para-metric variables. A paired t test was used for continuous variables. This is a descriptive study; results are presented as the mean±the standard deviation. All statistical analyses were performed using the SPSS 11 program; for statistical difference the Student t test and $p < 0.05$ was considered significant. Kaplan Meyer curve was applied where indicated.

Results

In the study were recruited 270 children aged between 5 and 16 years old with a mean age of 12.4 ± 4.5 years. ECG was done on 45% of the patients and transthoracic echocardiography on 100% of them. Surgery was indicated in 256 cases. Lesions of the valves needing prophylaxis with penicillin was diagnosed in 14 cases. In 95 patients surgical correction could not be performed because of three causes: financial limitation (61%, n=58), cultural beliefs (12.6%, n=12) and very advanced pathology (26.4%, n=25). Symptoms at presentation are listed in Table 1. The main symptoms registered were fatigue and shortness of breath on exertion.

Pattern of valvulopathies

Mitral valve regurgitation was the pathology the most encountered (61.5%, n=164), followed by post-rheumatic aortic valve regurgitation (38.5%, n=103), mitral valve stenosis, mitral valve disease, aortic valve stenosis and combined mitro-aortic valvulopathy were also represented. Tricuspid regurgitation with elevated pressure in the right ventricle as complication of mitral lesion was detected in 234 cases (87%).

Electrocardiogram

Left ventricular hypertrophy 47.3% was the most seen change on the ECG. Also were right ventricular hypertrophy 22.3%, left auricular hypertrophy 20.1%, right auricular hypertrophy 10.3%, left bundle branch block 57.7%, right bundle branch block 42.3%. Arrhythmias were represented with: sinus tachycardia 48.3%, atrial fibrillation 15.2%, ventricular premature contractions 19.4%, atrial premature contractions 17.1%.

Transthoracic doppler-echocardiogram

We could see during the echographic examination the fibrotic destruction of the mitral valve. The valves were calcified, immobile in case of stenosis, rigid with coaptation defect and retraction of the subvalvar apparatus in case of regurgitation. Complications of RHD observed included different stages of tricuspid regurgitation and elevated pressure in the right ventricle. The mean vena contracta was 13.2±2.1mm, the mitral valve annulus 3.6±1.8mm, the left atrium major axis 10.2±3.2mm, the minor axis 9±2.5mm. The left atrial volume was Giant left atrium was seen in 5 cases with a major axis 132±1.3mm, the minor axis 110±0.8 mm (Table 1). The mean diastolic diameter of the left ventricle (LVEDD),

Table 1 Symptoms of patients recruited in the study / <i>Symptômes des patients recrutés dans l'étude.</i>	
Symptoms	n
Shortness of breath on exertion	196
General fatigue	178
Orthopnea	92
Palpitations	152
Lower limbs swelling	161
Chest pains	84
Cough	43
Anorexia	78
Abdominal swelling	71
Epigastric pains	69

systolic diameter of the left ventricle (LVESD), the ejection fraction (EF), shortening fraction (SF) were respectively 56±3.5mm, 45±2.1mm, 56±4.5%, 25±2.3%. In patients with mitral regurgitation the effective regurgitant orifice area (EROA) was 0.27±0.7cm²; the regurgitation volume (RV) was -41.4±3.3ml/beat, the regurgitation fraction (RF) -38.7±2.1%. In patients with aortic regurgitation, the EROA was 0.151±0.8cm²; the RV was -38.2±2.3ml/beat, the RF -36.4±4.1%. In patients with aortic stenosis, the mean gradient was 45.3±1.8 mmHg, the aortic velocity 4.3±0.m/s, the aortic valve area 1.42±0.8cm². In patients with mitral stenosis, the valve area, the mean gradient, were 1.41±0.51cm², 12.4±2.7mmHg respectively. Patients in advanced stage were presenting with much dilated left ventricle with poor global contractility, low output and severe pulmonary hypertension (Table 2).

Complications

The main complication was congestive heart failure leading to re-hospitalization of children. Most of the patients on admission were in class III and class IV (37%) according to NYHA. Re-hospitalization rate was twice yearly in patients with advanced stage and yearly in other patients. Fatigue, shortness of breath, polypnoea, orthopnoea, lower limbs oedemas were at different levels was present in

Table 2 Echocardiographic parameters of patients in advanced stage / *Paramètres échocardiographiques des patients en stade avancé.*

	Non advanced pathology	Advanced pathology
LVEDD	42.2±2mm	63.1±3.1mm*
LVESD	25.3±1.2mm	51.2±2mm*
EF	68±3.2%	45±2.2%*
SF	40±2.2%	25±1.2%*
LVDV	200±3.1ml	310±2.9ml*
LVSV	120±3.2ml	280±2.2ml*
Vena contracta	8±1.2mm	11±2.2mm*
Tricuspid gradient	51±5.4mmHg	72±4.2mmHg*
TAPSE	12.2±1.2mm	8±2.2mm*
Mitral annulus	34.2±2.5mm	36.1±2.2mm
Tricuspid annulus	33.5±3.3mm	35±3.2mm
Left atrial volume	48±1.2ml/mm ²	63±4.2ml/mm ² *
Right atrial volume	37±2.2ml/mm ²	48±3.4ml/mm ² *

* p≤0.05; LVEDD: Left ventricular end diastolic diameter; LVESD: Left ventricular end systolic diameter; EF: Ejection fraction; SF: Shortening fraction; LVDV: Left ventricular diastolic volume; LVSV: Left ventricular systolic volume; TAPSE: tricuspid annular plane systolic excursion.

all children. Mortality in two years was 35% ($p \leq 0.05$, 95% CI=2.5 – 6.5), in five years was 65% ($p \leq 0.05$, 93% CI=2.7 – 7.21) Figure 1.

Cultural beliefs

Patients relieved with the therapy prescribed were reluctant to come for re-evaluation. The parents think that the problem of the child is mystical and the best work can be done only by traditional healers. Cardiac surgery for these parents is abomination since in their life ignoring the scientific progress; they haven't seen such things happening before. Religious parents will pray for child till the disease will exacerbate.

Discussion

Acute rheumatic fever and its complications is becoming a rarity in the western world; it is still non uncommon in the developing countries. In our study, we can see that the most affected population are very young people. Hillman ND et al reported surgery in children having a mean age of 13 ± 4 years old declaring that the incidence of post-rheumatic cardiopathies has increased in United States of America [8]. In Brazil the mean age at the time of first surgery was 12.0 ± 2.8 years [19]. We see that in Cameroon, Brazil or in United States of America, post-rheumatic valvulopathies are affecting almost the same population. On the TTE, the valves were rigid, calcified with coaptation defect in case of regurgitation, with a poor opening in case of stenosis [22]. We could observe a dilatation of all the chambers; in some cases, we observe a giant left atrium with a major axis dimension of 13 cm, with a volume of 68 ml/mm². The

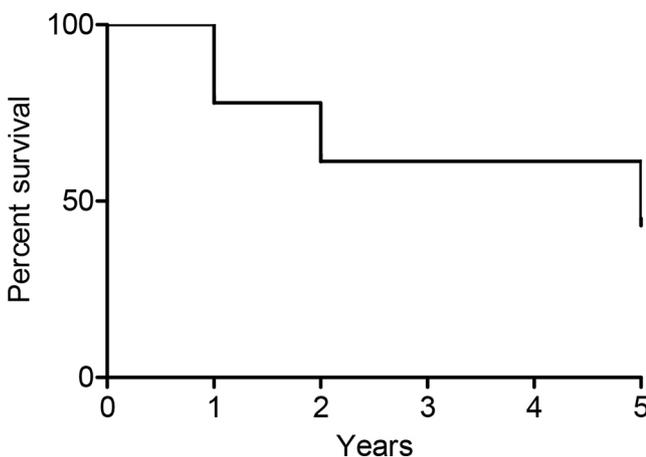


Fig. 1 Kaplan-Meier survival curve / La courbe de survie de Kaplan-Meier

pathology the most encountered was mitral valve regurgitation like in the study of Andréa Rocha e Silva et al in Brazil, in the study VALVAFRIC and in Uganda [10,12,19].

As in the study of Lubega S in Uganda, shortness of breath on exertion and fatigue were the main complaints of children presenting the first time for consultation [12]. Pulmonary hypertension was the complication present in advanced cases, indicative of the severity of the valvulopathy, the primary pathology of patients confirmed by Kingué S. et al in Valvafric in a huge cohort of patients in central and western Africa [10].

Chelo D. and al after a similar study reported that worldwide, about 470,000 cases of rheumatic fever are reported each year and nearly 233,000 deaths from rheumatic fever and rheumatic carditis. Poverty, poor sanitation and inadequate health systems promote rheumatic fever which results in valvular complications. They continued saying that there were more often already advanced cases and a study in the population would have shown significantly more subjects with rheumatic fever sequelae [5]. Marijon et al. who did screening in schools of Cambodia and Mozambique found that 2–3% of students were carriers of rheumatic valvular lesions. Almost all of these valvulopathies had not been diagnosed previously [13].

In our study, right ventricular dysfunction was present in many children, having a very low TAPSE. Right ventricular dysfunction may develop via multiple mechanisms:

- left ventricular failure which increases afterload by increasing pulmonary venous and ultimately pulmonary artery pressure, partly as a protective mechanism against pulmonary edema;
- left ventricular dysfunction may lead to decreased systolic driving pressure of right ventricular coronary perfusion, which may be a substantial determinant of right ventricular function;
- ventricular interdependence due to septal dysfunction may occur;
- left ventricular dilatation in a limited pericardial compartment may restrict right ventricular diastolic function [24].

One of the main complications of the valvulopathies was congestive heart failure as seen in the study Valvafric, and was present on first presentation of many patients [10]. In patients presenting with advanced congestive heart failure, mainly in class III and IV NYHA classification the echocardiographic parameters were objectively statistically worse: dilated ventricles, systolic dysfunction and severe pulmonary hypertension. The compensation treatment was started immediately after admission.

In our study, we see that in advanced cases five years mortality is 100%. High mortality has been seen in our study compare to the study of Jackson SJ et al - the highest mortality rates from post streptococcal glomerulonephritis and

rheumatic heart disease were reported in the indigenous populations of Australia (23.8 per 100 000) [9]. Among countries with vital registration data, the highest mortality was found in Mauritius (4.32 per 100 000). A large multinational African study demonstrated that RHD prevails as the most frequent cause of heart failure among children and young adults, and importantly that the 180-day mortality is as high as 17.8% [20,23]. In rural Ethiopia annual mortality rate reaches 12.5% among patients with RHD and as many as 70% of such patients die under 26 years of age 35 [7,16].

Surgery on time is very important, as well as prophylaxis and early detection of cases. There is an urgent need for comprehensive service frameworks to improve access and level of care and services for patients, educational programs to reinforce the importance of prevention and early diagnosis and a relevant research agenda focusing on the African context [21,26]. The Verdzev Foundation for the early detection and prophylaxis of post-rheumatic valvulopathies conceived a program called FARCI to tackle the disease in the BUI division of Cameroon. The program needs funding to start.

Conclusion

Post-rheumatic mitral valve regurgitation is the pathology the most encountered. Pulmonary hypertension is the most common complication of the disease. Five years mortality is very high and the need of educational programs to reinforce the importance of prevention and early diagnosis are urgent in our setting.

Conflict of interest: the authors do not have any conflict of interest to declare.

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