Prevalence of rheumatic heart disease in young adults from New Caledonia

Prévalence de la valvulopathie rhumatismale chez l’adulte jeune en Nouvelle-Calédonie

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Received 16 December 2013; received in revised form 25 June 2014; accepted 4 July 2014
Available online 12 December 2014

KEYWORDS
Rheumatic heart disease; Echocardiography; Public health; Screening; Adult

Summary
Background. — Rheumatic heart disease (RHD) is an important public health issue, particularly in the Pacific region, but its true burden is unknown.
Objectives. — To evaluate the prevalence of rheumatic heart disease (RHD) in young adults from New Caledonia, based on echocardiography, and to evaluate the accuracy of dynamic criteria, focusing on mitral valve (MV) leaflet motion.
Methods. — Blind analysis of echocardiography by three cardiologists; diagnosis of RHD required at least one dynamic criterion (exaggerated or restricted MV leaflet motion); subjects with morphological criteria (MV leaflet thickening), but without dynamic criteria, were considered as borderline.
Results. — There were 834 subjects from three socioeconomic groups, aged 18–22 years: 699 had normal echocardiography; 93 (11.5%) had physiological regurgitation; nine (0.9%) had borderline RHD; and five (0.59%) had RHD. The prevalence of RHD in New Caledonia was thus estimated at 5.9 per 1000 (95% confidence interval 2.6–12.2). The RHD cases were of Pacific

Abbreviations: AR, aortic regurgitation; CI, confidence interval; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; RHD, rheumatic heart disease.
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http://dx.doi.org/10.1016/j.acvd.2014.07.053
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Background

Rheumatic heart disease (RHD) is an important public health issue worldwide [1—4] and particularly in the Pacific region [5—9]. In many countries, school-based echocardiographic screening for RHD is being conducted [5,7—10]. These and other studies suggest that the prevalence of RHD increases steadily during the teenage years, peaking in young adults [11]. However, by not including older adolescents and young adults, school-based RHD screening programmes may underestimate the true burden of RHD in the population. Unfortunately, screening of adults is notoriously difficult, mainly because of low participation rates, but at least one study (in Nicaragua) has managed to screen for RHD in an adult population [10].

Echocardiography is a very sensitive tool for the screening of RHD, compared with cardiac auscultation [5,7,8]. The echocardiographical criteria required for the diagnosis of RHD have been debated [12,13], although the recent publication of the World Heart Federation criteria for echocardiographical diagnosis of RHD provides an evidence-based foundation for future research and practice [14]. The diagnosis of RHD requires the presence of Doppler criteria confirming pathological valvular regurgitation, and a range of morphological criteria.

MOTS CLÉS
Valvulopathie rhumatismale ; Échocardiographie ; Santé publique ; Dépistage ; Adulte

Résumé

Contexte. — La valvulopathie rhumatismale (VR) est une importante question de santé publique, particulièrement dans la région Pacifique, mais son vrai fardeau est inconnu.

Objectifs. — Évaluer la prévalence de la VR chez l’adulte jeune en Nouvelle-Calédonie, basé sur l’échocardiographie et évaluer la précision du critère dynamique, se concentrant sur les mouvements des feuilles de la valve mitrale (VM).

Méthode. — Analyser en aveugle des échocardiographies par trois examinateurs ; le diagnostic de VR requérant au moins un critère dynamique (mouvement exagéré ou restrictif d’un feuillet de la VM) ; les sujets avec des critères morphologiques (épaississement de feuillet de la VM), mais sans critère dynamique, sont considérés comme borderline.

Résultats. — Sur les 834 sujets des trois groupes socio-économiques, âgés de 18 à 22 ans : 699 avaient une échocardiographie normale ; 93 (11,5 %) avaient une fuite physiologique ; neuf (0,9 %) une VR borderline ; et cinq (0,59 %) une VR avérée. La prévalence de la VR en Nouvelle-Calédonie a été ainsi estimée à 5,9 pour mille (95 %, intervalle de confiance 2,6–12,2). Les cas de VR sont de l’ethnicté Pacifique. Les fuites physiologiques étaient plus fréquentes chez les sujets du Pacifique (13,7 %) que chez les sujets non-Pacifique (6,9 % ; p < 0,0001). La VR était plus importante dans le groupe socio-économique le plus défavorisé. Aucun désaccord n’est survenu par les trois examinateurs concernant l’analyse du critère dynamique ; l’ensemble des désaccords étaient relatif aux critères morphologiques.

Conclusions. — La prévalence de la VR diagnostiquée échocardiographiquement est estimée chez l’adulte en Nouvelle-Calédonie à 5,9 pour mille ; sont plus touchés les sujets d’ethicité Pacifique et ceux à bas niveau socio-économique.

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Table 1 Echocardiographical criteria used for the diagnosis of rheumatic heart disease [14].

<table>
<thead>
<tr>
<th>RHD diagnosis categories</th>
<th>Normal echocardiography</th>
<th>Physiological regurgitation</th>
<th>Borderline RHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria</td>
<td>No valvular regurgitation and no MS</td>
<td>Valvular regurgitation, without all four Doppler criteria and without morphological criteria</td>
<td>Pathological valvular regurgitation, with at least one morphological static criterion, but without dynamic criteria</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No valvular regurgitation, with morphological criteria, but without dynamic criteria</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Pathological regurgitation and at least one dynamic criterion or MS</td>
</tr>
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**Doppler criteria (the diagnosis of pathological valvular regurgitation [e.g. non-physiological] required all four criteria)**
- Holosystolic (MR) or holodiastolic (AR) jets (with homogeneous spectral envelope on at least three consecutive cardiac cycles)
- Peak velocity ≥ 3.5 m/s
- Seen in two views
- Regurgitation jet length ≥ 2 cm (in at least one view)

**Morphological criteria**
- **Static criteria: MV**
  - Retraction or thickening of chordal/subvalvular apparatus
  - AMVL thickening ≥ 3 mm
  - Thickening of aortic cusp
- **Dynamic criteria: MV**
  - Coapitation defect
  - Decreased mobility of PMVL, with normal mobility of AMVL: false prolapse of AMVL (leading to a posterior direction of MR jet)
  - Decreased mobility of AMVL tip (dog-leg or MS aspect)
  - Excessive mobility of AMVL or PMVL: valve prolapse due to chordal elongation or chordal rupture

**Table 1 (Continued)**

<table>
<thead>
<tr>
<th>Dynamic criteria: AV</th>
<th>Restricted motion in opening</th>
</tr>
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</table>

Participating in the programme, on the basis of their own expertise. Using this method, the prevalence of RHD in 10-year-old children has been found to be approximately 13 per 1000 (unpublished data from Agence Sanitaire de New Caledonia).

Because the prevalence of RHD in adults in New Caledonia is unknown, we conducted a prospective echocardiographical screening study to evaluate the prevalence of RHD among young adults (aged 18–22 years) from New Caledonia. Our secondary aims were to identify high-risk subgroups as screening targets for future prevention programmes and to evaluate the accuracy and reproducibility of the echocardiographical criteria we used for the diagnosis of RHD, putting special emphasis on the dynamic analysis of MV leaflet motion.

**Methods**

**Study design and participants**

New Caledonia is administratively divided into three provinces: North, South and Islands. The population is 246,000, with two-thirds living in Nouméa and its suburbs in the South Province [16]. The population of New Caledonia includes people of Pacific ethnicity (Melanesians, 44%; Polynesians, 14% [composed of Wallisians, Futunians and French Polynesians]) and non-Pacific ethnicity (Caucasians, 34%; Asians, 8%).

The population of people aged 18–22 years is estimated as being 13,500 in the South Province [16], and they can be divided into three distinct groups: 6480 (48%) are students; 3645 (27%) are workers or apprentices; and 3375 (25%) are non-school and unemployed (this is the lowest socio-economic group, who frequently live in tribal villages or shanty towns) [16].

**Sampling**

Based on an anticipated RHD prevalence of 30 per 1000, the minimum sample size required was 1250 for a 95% confidence interval (CI) of ± 10 per 1000.

We aimed to sample the three groups roughly according to their distribution in the population, as reported in the 2009 census supplied by Institut de la Statistique et des Études Économiques (ITSEE) [16]. The group of students (group 1, n = 596) was composed of subjects randomly
selected from an enrolment list obtained from universities; the group of workers (group 2, \( n = 335 \)) was composed of subjects randomly selected from a list of apprentices in the Chamber of Commerce of Nouméa or from the Department of Occupational Medicine of New Caledonia; the group of out-of-school and unemployed subjects (group 3, \( n = 339 \) subjects) was planned to be composed of subjects recruited using purposive sampling by our local social workers’ network.

Ethics approval was obtained from the Public Health Authorities of the South Province. Information about the study and RHD was provided to the institutions involved and to sampled subjects. Written informed consent was obtained from all participants before screening was performed.

Vital status on 31st December 2012 was checked in the national register; no patient with RHD died during the follow-up period (median 2.3 years).

**Screening procedure**

Personal or familial past history of acute rheumatic fever or RHD was recorded by asking the participants. The subject’s ethnic group was defined by the subject. Cardiac auscultation was not performed.

All echocardiographical examinations were performed by a single operator (investigator 1), between May and December 2010, in either an infirmary or a dedicated classroom, using a Vivid iTM (GE Healthcare, Freiburg, Germany) portable cardiac ultrasound machine and a multifrequency 3S adult probe (1.9–3.8 MHz).

A standard protocol was used for the acquisition, recording and storage of echocardiographical data. Imaging was performed in standard parasternal long and short axis, and apical four-chamber views. Depth, sector size and gain were optimized to achieve maximal frame rate and resolution; a second harmonic frequency was used if needed. Colour Doppler was used with the highest aliasing velocity allowed by the machine; pulsed and continuous Doppler were used to assess velocity and the spectral envelope of transvalvular flow and regurgitations.

**Reading of echocardiograms**

A blind and separate analysis was performed by the three investigators, reviewing stored images directly on the echocardiography machine; in case of disagreement, the final diagnosis was established by consensus between the investigators. Each reader was asked to categorize each echocardiogram as normal, physiological regurgitation, borderline RHD or definite RHD, according to predefined criteria established by our group in 2009, before the World Heart Federation RHD criteria were published and became the gold standard for RHD screening in 2012 (Table 1).

In contrast to the World Heart Federation criteria, we required the presence of at least one dynamic criterion to accept the diagnosis of definite RHD; in the absence of abnormal MV leaflet motion, or even in the presence of one or several static morphological criteria (leaflet thickening and/or subvalvular apparatus retraction), the case was labelled as ‘borderline RHD’.

In case of an abnormal echocardiogram, the patient was referred to their primary care doctor for further management.

**Statistical methods**

Data were entered and analysed using Microsoft Office Excel 2007 software. Prevalence rates and confidence intervals were computed using binomial probability tables. Fisher’s exact test was used to compare prevalence rates between groups. Cohen’s Kappa coefficient was calculated according to the referenced method [17].

**Results**

**Sampling of the population**

The total number of subjects sampled was 1161; the number of subjects sampled for group 1 (\( n = 717 \)) and group 2 (\( n = 390 \)) were in agreement with the number of subjects determined with respect to our stratification plan (596 and 335 subjects, respectively, for groups 1 and 2). However, we had difficulty recruiting for group 3, and managed to enrol only 54 of the 339 subjects planned (15% [or 7% of the total study population]); all of these subjects were sampled from a list of 104 prisoners obtained from the prison in Nouméa (Table 2).

Of the 1161 subjects sampled and invited to participate to our study, 834 finally had an echocardiographical examination: 280 subjects were absent on the day of screening and 47 subjects refused to participate for personal reasons (four of these subjects reported that they already had RHD). Participation rates as a proportion of those invited to participate were 70% for group 1, 72% for group 2 and 100% for group 3.

Of the 834 subjects included, there were 451 (55%) men and the mean age (± standard deviation) was 20.0 ± 1.5 years; 517 (62%) subjects were from the Pacific.
community, including Melanesians (n = 382, 46%) and Polynesians (n = 135, 16%); 317 (38%) subjects were from the non-Pacific community (Asians, n = 34; Caucasians, n = 283) (Table 3).

### Echocardiographical results

Of the 834 subjects examined, 699 were normal (83.6%), 93 had physiological mitral regurgitation (MR) and/or aortic regurgitation (AR) (11.5%), 28 had non-rheumatic heart disease (3.4%), nine had borderline RHD (0.9%) and five had definite RHD (0.6%) (Table 3). The prevalence of definite RHD in our population was therefore estimated at 5.9 per 1000 (95% CI 2.6—12.2).

Twenty-eight participants (3.4%) had non-rheumatic cardiac abnormalities, many of which were minor (Table 4).

The rate of physiological regurgitation was significantly higher in subjects of Pacific ethnicity (71/517, 13.7%) than in those of non-Pacific ethnicity (22/317, 6.9%) (odds ratio 2.39, 95% CI 1.41—4.10; P = 0.0001).

### Characteristics of subjects with rheumatic heart disease

Of the five subjects with definite RHD (three of whom were men), one had been diagnosed previously as having RHD at the age of 11 years; none of the other four reported any previous history of acute rheumatic fever or RHD.

One subject had pure severe mitral stenosis (MS) with a mean gradient of 10 mm and mild AR; two subjects had mixed MV disease (mild MS and MR) associated with mild AR; and two subjects had mild MR and AR. In all subjects, MR was due to a restricted systolic motion of the posterior MV leaflet, with normal systolic motion of the anterior MV leaflet (false prolapse of anterior MV leaflet), with a posteriorly directed MR jet.

All five definite RHD cases were of Pacific ethnicity (Melanesian, n = 4; Polynesian, n = 1), giving a prevalence of definite RHD in Pacific subjects of 9.7 per 1000 (95% CI 4.3—19.7). The difference in prevalence between Pacific and non-Pacific participants did not reach statistical significance for definite, borderline or all RHD.

The prevalence of RHD was higher in group 3 (18.6 per 1000, 95% CI 4.5—66) than in group 1 (6 per 1000, 95% CI 2.6—12) or group 2 (3.6 per 1000, 95% CI 0.9—13), although the difference was not statistically significant when groups 1 and 2 were pooled and compared with group 3. However, all borderline cases were found in groups 1 and 2.

### Interobserver reproducibility

The global Kappa coefficient between the three observers was 0.62 (Z = 17.9; P < 0.0001), indicating good interobserver reliability.

All five cases of RHD were correctly identified by the three reviewers during separate analyses; thus, there was no disagreement between reviewers concerning dynamic criteria.

In contrast, in six out of nine borderline subjects, the separate analysis was discordant between the investigators. In all six cases, the discordance related to the presence of morphological criteria rather than regurgitation: observer A, two cases; observer B, one case; observer C, three cases; all these cases were finally classified as borderline during consensual review.

### Discussion

Based on a systematic echocardiographical screening of 834 young adults, aged 18—22 years, we estimated the prevalence rate of definite RHD in New Caledonia to be 5.9 per 1000. However, all RHD cases, and most borderline RHD cases, were in people of Pacific ethnicity, resulting in a prevalence of almost 1% (9.7 per 1000) for definite RHD in
this group. Our study also found a much higher rate in prisoners (19 per 1000), who formed the group with the lowest socioeconomic status in this study. Hence, Pacific ethnicity and low socioeconomic status appear to be associated with an increased risk of RHD in New Caledonia. In contrast, borderline cases were not found in the lowest socioeconomic group, and in lower proportions in Pacific participants than cases of definite RHD. The lack of classical epidemiological associations in this group suggests that many of the cases in the borderline RHD category do not represent true RHD.

There are no comparable studies of RHD screening in adults in the Pacific. However, in Nicaragua [10], a systematic study based on echocardiography was performed in adults, and reported a rate of RHD of 22 per 1000. However, in this study, the criteria for RHD were less strict than ours; specifically, definite RHD could be confirmed in the Nicaragua study in the absence of any dynamic morphological criteria, which we suggest is a useful means of avoiding overdiagnosis of RHD.

Screening programmes for adults are often affected by low participation rates, thought to be due to factors such as availability, as a result of employment, or lack of interest. We were pleasantly surprised by the fact that approximately 70% of students and workers agreed to participate. This indicates a high level of interest and possibly awareness of RHD among educated and working people in New Caledonia. However, screening the subgroup of indigenous unemployed people proved to be very difficult. This group of people live spread out in tribal villages or shanty towns, and are frequently overlooked, even by the specialized social workers’ network. We finally had to resort to sampling through the prison. Given that this group represents those with the lowest socioeconomic status and the highest rate of RHD, developing strategies to ensure their participation will be an important prerequisite for any routine adult RHD screening programme in future.

The prevalence rate of RHD in our study is lower than the prevalence found to date in school-age child screening in New Caledonia (13 per 1000), although the child surveys used non-standardized echocardiographical criteria. It is possible that the prevalence of RHD in children might have been overestimated in those studies; when faced with a doubtful case in a child, many cardiologists from New Caledonia err on the side of caution, diagnose RHD and begin secondary prophylaxis with benzathine penicillin, aiming to prevent evolution towards more severe RHD. This strategy has been advocated by Marijon et al. on a large scale [7], but the benefit of this approach needs to be clarified, given that it exposes many children to long and painful treatment. Moreover, although penicillin is cheap, ensuring adherence to monthly prophylactic injections over several years consumes a lot of already limited healthcare resources. In New Caledonia, it has been estimated that only 40% of patients are fully compliant with monthly benzathine penicillin injections each year [15].

We found lower rates of RHD in New Caledonian adults than have been described in Pacific island studies in children. For example, rates in school-age children using echocardiographical screening have been reported at 24 per 1000 in New Zealand [9], 43 per 1000 in Tonga [5] and 55 per 1000 in Fiji [8]. This difference may be due to the different age groups examined: the Nicaraguan study found a slightly lower prevalence of RHD among adults than school-age children [10], although among Aboriginal Australians, the prevalence in adults aged 15–34 years is much higher than the prevalence in those aged 5–14 years [11]. Other potential explanations for the difference include sampling issues (we undersampled people in the lowest socioeconomic groups), our highly specific echocardiographical criteria and the rigorous methodology using independent readings by three cardiologists. We note that the new World Heart Federation criteria [14] are also highly specific and are quite similar to the criteria we used, so we suspect that future prevalence studies using those criteria will find slightly lower rates than have been reported in the last few years in many developing countries.

In our study, we decided to systematically increase the specificity of the diagnosis of RHD, starting with strict optimization of the settings of the machine during image acquisition. The colour Doppler velocity was set at the highest level to avoid overestimation of the colour Doppler jet extension. In contrast to the combined criteria proposed by Marijon et al. [12], our algorithm required the presence of pathological regurgitation (unless MS was present) for the diagnosis of RHD. Moreover, all pathological regurgitation are not rheumatic [13]: using strict criteria, we identified a significant subgroup of patients (14 subjects, 16.8 per 1000) with non-rheumatic pathological MR or AR due to valve dysplasia or minor congenital abnormalities. The rate of non-rheumatic pathological valvular abnormalities should be reported clearly in every study to ensure that this kind of overestimation of RHD is avoided.

It is generally accepted that some degree of MV chordal shortening (and hence valvular motion restriction) is almost always present in established RHD [14]. Hence, in most studies, ‘chordal shortening’, and ‘mitral subvalvular apparatus thickening’ are accepted as major morphological criteria for the diagnosis of RHD [7,8,10,11]. However, chordal shortening or thickening are obviously subjective criteria. Therefore, we proposed to analyse the direct consequence of chordal retraction, represented by the limitation of the motion of MV leaflets, helped (if needed) by its surrogate marker, MR jet direction. In all our RHD cases, we observed a previously described typical pattern, combining restriction of the mobility of the posterior MV leaflet with preserved mobility of the anterior MV leaflet, leading to a posteriorly directed MR jet (‘false prolapse of anterior MV leaflet’) [14–18]. In our view, the diagnosis of RHD must be seriously questioned if any degree of mitral false prolapse cannot be demonstrated.

The analysis of dynamic criteria proved to be highly concordant between the three reviewers. Indeed, there was no disagreement between our three reviewers concerning the analysis of the dynamic criteria. In contrast, all six disagreements between the reviewers concerned the presence or absence of one morphological static criterion; those six cases were finally considered to be borderline cases after consensual review. Further refinements of the diagnostic criteria should perhaps emphasize the importance of the dynamic criteria, given that these appear to be the most reproducible between different reviewers.

The prevalence of physiological MR and/or AR was 11.5%, within the range of what has been reported in previous studies [19]. However, the prevalence of physiological
regurgitation was significantly higher in the Pacific community (13.7%) than in the non-Pacific community (6.9%; \( P < 0.0001 \)); to the best of our knowledge, such a trend has not been reported before. As the Pacific community is also most affected by RHD, the existence of some link or continuum between RHD and physiological regurgitation, as suggested by Marijon et al. [12], is possible. Determining the risk of these cases of mild physiological regurgitation later degenerating to significant RHD will require longitudinal follow-up in highly endemic countries.

A major challenge facing the New Caledonia health care system is ensuring that RHD patients, such as those detected in this study, receive appropriate care – indeed this is a prerequisite for embarking on a screening programme. In New Caledonia, it has been estimated that only 40% of subjects prescribed monthly injections of benzathine penicillin for secondary prophylaxis actually receive all the 12 planned injections each year [15]. Clearly, there is work to do in New Caledonia to strengthen this critical element of RHD control.

Study limitations

We were not able to enrol the expected 1250 participants. Echocardiographical screening for subclinical RHD among young adults is not easy because some groups (non-schooled, not job seekers) are difficult to reach; this is an important obstacle to overcome, because the rate of RHD is very high (18.6%), and it probably explains why borderline RHD was not found in group 3.

Conclusions

We conclude that RHD in New Caledonia causes a significant burden in adults, particularly in those of Pacific ethnicity and low socioeconomic circumstances. This high-risk group should be the preferred target for further interventions aimed at controlling the RHD disease burden, potentially including systematic screening in New Caledonia. Our study suggests that the prevalence of RHD may be lower in New Caledonia than in other neighbouring Pacific Islands, although this requires confirmation in further studies. Our results also suggest that the analysis of dynamic criteria, focusing on the analysis of MV leaflet tip mobility, is more accurate, reproducible and specific than the standard morphological criteria.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Acknowledgements

This study was supported by the South Province of New Caledonia. We are anxious to thank the following for supporting them in this venture: Vice-Rectorat, DDEC and University (student’s group); Consular Chambers (CCI, CFA, CA, EGC) and SMIT (worker’s group); Provincial Services and Detention Centre (non-schooled, unemployed group). We would also like to thank Dr. Laurence Yamamoto for initial help with the translation, and Dr. Sylvie Lomont and Mariana Mirabel for the follow-up.

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