The 2020 Guideline for the prevention, diagnosis, and management of acute rheumatic fever and rheumatic heart disease (3.2 edition, March 2022)

Update Brief: Management of borderline RHD with secondary prophylaxis

Process for updating the Guideline

Information in the 2020 Guideline for prevention, diagnosis, and management of acute rheumatic fever (ARF) and rheumatic heart disease (RHD) remains current through the review of published research and clinical practice data. The Guideline Implementation Plan outlines the process for updating the Guideline which includes a robust assessment of new and emerging evidence by a group of experts and consideration of implications for practice and policy. The expert group makes recommendations to RHDAustralia based on the significance and relevance of the evidence in the Australian context. The decision-making process for Guideline changes is consistent with the Guideline Development Framework used for the 3rd edition, and is in accordance with NHMRC Clinical Guideline Standards.

Previous Recommendation (3rd edition, February 2020)

For high-risk individuals aged 20 years of age of less who have no documented history of ARF and are diagnosed with borderline RHD on echocardiogram, secondary prophylaxis was not routinely recommended, but considered in some circumstances, including family preference, with family history of rheumatic heart valve surgery, or with suspected retrospective history of ARF.

New evidence

In November 2021 the results of the *GwokO Adunu pa Lutino* (GOAL) study were published. This was a large, randomized controlled trial of secondary antibiotic prophylaxis in Ugandan children and adolescents aged 5 to 17 years with latent RHD[1]. Latent RHD includes both definite (mild) and borderline asymptomatic RHD. Among participants who had borderline RHD at baseline, one person of 318 (0.3%) in the prophylaxis group had echocardiographic progression at 2 years, compared to 25 persons of 333 (7.5%) in the control placebo group.

Expert assessment group

The impact of using secondary prophylaxis in the management of borderline RHD in children and adolescents was considered by an Australian expert assessment group. This group consisted of specialist physicians and paediatric cardiologists working in the NT, Qld, SA, and United States including Prof Anna Ralph, Prof Bart Currie, Dr Ben Reeves, Dr Bo Remenyi, Dr Dan Engelman, Dr Gavin Wheaton, Dr James Marangou, Dr Joshua Francis, Dr Andrea Beaton, and Ms Vicki Wade.

Updated Recommendations (Guideline 3.2 edition)

For individuals aged 20 years of age of less who have no documented history of ARF, are diagnosed with borderline RHD on echocardiogram and who live in a high-RHD risk setting[2], secondary prophylaxis should be provided for a minimum of two years following diagnosis. Medical review and repeat echocardiogram should be conducted at 1-2 years after diagnosis, and again 1-2 years after ceasing secondary prophylaxis.

Ceasing secondary prophylaxis should be considered if all the following three scenarios exist:[1]

1. no evidence of probable or definitive ARF within the last 10 years,
2. normalization of the echocardiogram at 2 years after diagnosis, or anytime thereafter, and
3. no echocardiographic progression of borderline RHD to definite RHD.

[1] Refer Guideline Table 10.2, page 168

The recommendation to treat people in Australia with borderline RHD should take effect from this point forward, and not impact the current management plans for people already diagnosed with borderline RHD.

Discussion

Borderline RHD is thought to represent both a combination of normal variations in heart echocardiogram findings and early RHD pathology. It is defined as *echocardiographic features which are abnormal but do not fulfil criteria for the diagnosis of RHD*. Therefore, a change to recommendations that children and adolescents should receive four weekly benzathine benzylpenicillin intramuscular injections for two years, when in some cases the echocardiogram findings are normal variations, was not taken lightly. Potential adverse effects of the medication and the impact on children and family life were carefully considered.

Results of the GOAL study are applicable to the Australian RHD context and could have implications for Australian children. The results show that in some cases of borderline RHD, progression of disease may be interrupted using secondary prophylaxis. This was also found to be the case in participants who had definite latent RHD. As such, the following points were addressed by the expert assessment group:

- **The duration of secondary prophylaxis** for borderline RHD is two years, which was the timeframe in the GOAL study.
- **The age group** is 20 years or less, which aligns with the World Heart Federation definition of borderline RHD.
- **The high-risk setting** caveat is due to the prevalence of borderline RHD which has been found to be significantly higher in high-risk settings compared to low risk settings[2].

Practice implications/challenges

Any change to the Guideline is likely to impact the function of jurisdictional registers (for example, the data collection and reporting capabilities of the registers vary from jurisdiction to jurisdiction depending on jurisdictional requirements, resources, IT infrastructure) and may have resource implications for the jurisdictional RHD Control Programs and service providers. Administering secondary prophylaxis in a timely manner is already challenging, and the implications of diagnosing a borderline RHD case with these new recommendations will increase the burden on the patient and family, increased injection delivery, and place greater demands on resourcing of treatment including medical reviews and echocardiograms. RHDAustralia will work through the implementation issues with the jurisdictional RHD Control Programs and others providing service delivery.

Specificity of echocardiography reporting of borderline RHD

The diagnosis of borderline RHD can sometimes be challenging due to the required qualitative assessment of some of the World Heart Federation criteria[3,4]. The expert assessment group recognizes the limitations of interpreting subtle valvular changes in asymptomatic, high-risk populations. Widespread and consistent application of the criteria and a standardized reporting approach is encouraged, to provide the most reproducible and accurate detection of borderline RHD.

The World Heart Federation 2012 criteria for echocardiographic diagnosis of RHD are currently being updated and due to be published in 2022. RHDAustralia will announce the publication of this and any subsequent changes to the Australian Guideline after a period of review.

References

1. Beaton A, Okello E, Engelman D, et al. Determining the impact of Benzathine penicillin G prophylaxis in children with latent rheumatic heart disease (GOAL trial): Study protocol for a randomized controlled trial. *Am Heart J* 2019; 215: 95-105.

2. Roberts K, Maguire G, Brown A, et al. Echocardiographic screening for rheumatic heart disease in high and low risk Australian children. *Circulation*. 2014; 129(19): 1953-61.

3. Scheel A, Mirabel M, Nunes MCP, et al. The inter-rater reliability and individual reviewer performance of the 2012 world heart federation guidelines for the echocardiographic diagnosis of latent rheumatic heart disease. *Int J Cardiol*. 2021; 328: 146-51.

4. Bacquelin R, Tafflet M, Rouchon B, et al. Echocardiography-based screening for rheumatic heart disease: What does borderline mean? *Int J Cardiol*. 2016; 203: 1003-4.

5. Remenyi B, Wilson N, Steer A, et al. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease – an evidence-based guideline. *Nat Rev Cardiol.* 2012; 9(5): 297-309.

6. Beaton A, Zühlke L, Mwangi J, Taubert KA. Rheumatic heart disease and COVID-19. *Eur Heart J*. 2020; 41(42): 4085-86.