Original article

Economic evaluation of screening for familiar form of arrhythmogenic right ventricular cardiomyopathy in Poland

Ewa Kowalik, Elżbieta K. Włodarska, Olgierd Woźniak, Piotr Hoffman

Department of Congenital Heart Diseases, National Institute of Cardiology, Warsaw, Poland

Abstract

Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a myocardial disease associated with fibrofatty tissue replacement in heart muscle leading to arrhythmia, heart failure or sudden death (SCD) often being the first manifestation in probands. At least 50% of cases of ARVC are inherited.

Aim: To evaluate costs and cost-effectiveness of diagnosis of the disease in asymptomatic relatives in Poland.

Methods: 239 asymptomatic subjects (mean age 35 years, 120 male) belonging to 42 families affected with ARVC were examined between May 2003 and May 2005. The costs of outpatient visits and additional diagnostic tests were included. Payer perspective was used.

Results: In all individuals ECG and transthoracic echocardiography were performed. Magnetic resonance imaging and signal-averaged ECG were performed in 35 patients suspected of having ARVC. The diagnostic criteria for ARVC were fulfilled in 29 patients and 57 subjects were recognised borderline. Total costs of screening amounted to 71 090 PLN (approximately 20 000 euro). The average cost per one case of detected ARVC was 2451 PLN (approximately 680 euro).

Conclusions: Costs of early detection of ARVC in individuals with a family history of the disease in Polish settings are low. Due the avilability of primary prevention of SCD the family screening in asymptomatic subjects is a cost-effective procedure.

Key words: cardiomyopathy, screening, cost-effectiveness

Kardiol Pol 2007; 65: 1442–1446

Introduction

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a primary disease of heart muscle in which the muscle of RV (in advanced clinical cases the pathological process also affects the left ventricle) is replaced by fibrous and adipose tissue causing electrical instability and contractility abnormalities.

The clinical symptoms predominantly include ventricular arrhythmia (the first symptom can be sudden death) and, in patients with severe heart muscle damage, symptoms of RV failure [1]. Arrhythmogenic cardiomyopathy is the second, after hypertrophic cardiomyopathy, cause of sudden cardiac death (SCD) among athletes and young, previously healthy people [2].

The disease, in at least 50% of cases, is genetically determined [3] and is inherited in an autosomal dominant manner (with the exception of Naxos disease – a form of ARVC inherited as an autosomal recessive condition). So far several genes have been identified, including the gene for the ryanodine receptor and desmosome proteins (desmoplakin, plakofilin, plakoglobin), whose mutations are responsible for different types of cardiomyopathy.

Currently genetic examinations are not used for ARVC detection. The diagnosis is based upon criteria of the ARVC Working Group [4].

The aim of this study was the evaluation of the costs and cost effectiveness of screening studies for detecting familiar forms of ARVC in a group of asymptomatic relatives of patients with ARVC in Poland.

Methods

Study group

A group of 239 apparently healthy relatives, belonging to 42 families with diagnosed ARVC, were examined in the

Address for correspondence:
Ewa Kowalik MD, Klinika Wad Wrodzonych Serca, Instytut Kardiologii, ul. Alpejska 42, 04-628 Warszawa, tel.: +48 22 343 42 63, e-mail: ewa.kowalik@gmail.com

Received: 19 April 2007. **Accepted:** 10 October 2007.

period between May 2003 and May 2005. There were 120 men and 119 women, aged 15-84 years (mean 35). The study group included relatives of those patients who agreed to inform their families about the disease and agreed to participate in diagnostic examinations. The screening included all relatives who agreed to participate in the study, irrespectively of the degree of the relationship (first-degree relatives or second-degree relatives). The members of the family were not accessed directly, respecting the patient's right to keep their disease secret.

The range of the studies

In all patients, during the outpatient visit, the interview and physical examination were conducted and resting ECG and transthoracic echocardiogram (TTE) were performed. In selected subjects, signal-averaged ECG in search of late potentials as well as magnetic resonance imaging were executed.

Screening algorithm of families affected with ARVC

Since there are no generally accepted guidelines regarding the screening procedures for familiar form of the disease, we used our own screening algorithm used for families affected with ARVC, created and used in our Department. Suggested algorithm of the screening examination is presented in Figure 1.

Diagnosis of ARVC

Diagnosis of ARVC was based on the presence of two major criteria, one major and two minor criteria or four minor diagnostic criteria published by the ARVC Working Group of the European Cardiologic Society and IFSC [4]. The presence of three minor and one major criteria was deemed necessary to detect the marginal form of this cardiomyopathy.

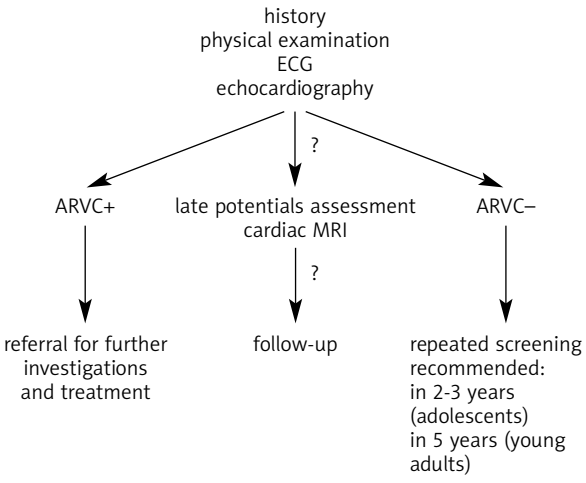

Figure 1. Proposed algorithm of screening in families affected with ARVC

Economic evaluation

The economic evaluation was based only on direct medical costs of the screening examinations and included the costs of the outpatient visit and the costs of additional examinations. The individual costs of particular medical procedures (including costs of medical staff work, costs of used materials and equipment amortisation) are described in Table I.

An effectiveness unit in economic evaluation was defined as the recognition of one case of familiar form of ARVC. The study was carried out from the perspective of the medical services payer.

Statistical analysis

The sensitivity analysis regarding the probability of detecting ARVC and marginal form of the disease was carried out using the bootstrap method (10 thousand bootstrap samples) [5]. The borders of confidence intervals were estimated with the percentile method.

Results

In all 239 relatives of patients diagnosed with ARVC the interview and physical examinations were conducted at the outpatient visit. Moreover, in all examined subjects resting ECG and TTE were performed. Subsequently, 35 relatives with the suspicion of ARVC were referred for

Table I. Individual costs [Polish zloty, PLN] of the outpatient visit and diagnostic tests (prices according to the Institute of Cardiology)

Medical procedure	Individual cost [PLN]*
Outpatient visit	80
Electrocardiogram	35
Transthoracic echocardiogram	100
Late potentials measurement	90
Cardiac magnetic resonance imaging	473

** 1 euro = 3.6 PLN*

Table II. Total costs [Polish zloty, PLN] of screening examinations

Medical procedure	Number of examinations	Total costs [PLN]*
Outpatient visit	239	19 120
Electrocardiogram	239	8 365
Transthoracic echocardiogram	239	23 900
Late potentials measurement	35	3 150
Cardiac magnetic resonance imaging	35	16 555
Total	–	71 090

** 1 euro = 3.6 PLN*

cardiac magnetic resonance imaging and late potentials measurement.

Eventually, the diagnostic criteria deemed necessary for ARVC detection were found to be fulfilled in 29 subjects aged 16-65 years (mean 35). In another 57 subjects the marginal form of the disease was diagnosed.

The total costs of screening examinations (the costs of outpatient visits and additional examinations) were 71 090 PLN. The costs of imaging examinations were 51 970 PLN, of which the major costs were the costs of echocardiographic examinations (33.62% of all screening costs). Table II presents partial costs and the total cost of all examinations performed to diagnose ARVC.

The mean cost of detecting one case of familiar form of ARVC was 2451 PLN in the presented screening study. The cost-effectiveness ratio for recognising one case of ARVC or the marginal form of the disease was, however, much lower and was 827 PLN.

The sensitivity analysis revealed that the 95% confidence limits for the mean cost of recognising one case of ARVC were 1964-3433 PLN.

Discussion

Arrhythmogenic right ventricular cardiomyopathy is not common, but it represents one of the main causes of SCD in younger age groups. The risk factors for SCD in these patients include progressive changes of the RV and left ventricular involvement. The approach to patients with ARVC includes cessation of excessive participation in sports and the management of ventricular arrhythmias.

So far, reports on the economic analysis regarding affordability of screening for familiar form of ARVC have not been published. Screening examinations for several conditions, including ARVC, are carried out on a larger scale in athletes. In Italy, such a system has been working for more than 25 years now and annually almost 6 million people who participate in training activities are examined, accounting for about 10% of the country's population [6]. Except for the interview and physical examination that are conducted, resting ECG is also performed. In the US, due to the very large population of subjects that are examined (10-15 million people participating in sports) and therefore high costs of the screening procedures, resting ECG is no longer performed [7].

In Western Europe the cost of consultation with a sport medicine specialist and the cost of the ECG for the screening procedure is around 30 euro [8], which is comparable with the cost of a specialist visit and ECG in the presented analysis performed in Polish conditions.

The cost-effectiveness of the echocardiographic examination (both the entire examination and with the use of portable echocardiographs) performed as the screening procedure in the detection of heart diseases associated with SCD, including ARVC, has not been assessed yet.

It should be emphasised that the population examined in our study is at greater risk of SCD than the general population of athletes (1 case in 100 thousand sportsmen annually [9]). Therefore, it can be indirectly concluded that the cost of detecting the disease is low and the possibility to use primary prevention substantially decreases the risk of SCD in subjects with familiar history of ARVC.

The data on the clinical and economic benefits of using the implantable cardioverter-defibrillator in primary prevention in high-risk patients with long QT syndrome and hypertrophic cardiomyopathy [10] indirectly show that the screening costs are effective also in relatives of patients with ARVC.

The described procedure is therefore potentially highly beneficial. Prospective studies are, however, needed for a complete economic evaluation (that is, estimation of the costs of avoiding death or gaining an additional year of life) of screening examinations for familiar forms of ARVC.

Study limitations

The presented study was the first one conducted in Poland in the population of subjects who were informed by the probands about their disease and who agreed to participate in screening examinations. The examination was performed in all relatives who entered the programme. The percentage of people who refused to have the examinations conducted as well as the number of probands who concealed their disease is not known. The results of the cost-effectiveness analysis could have been different if the screening was performed in the entire population of family members of patients with ARVC.

The cost analysis was based upon direct costs of medical procedures of the medical centre conducting the screening examinations for ARVC. The cost of the medical staff work is significantly lower in Poland compared with countries of Western Europe, which also affects the results of the presented analysis.

References

1. Corrado D, Basso C, Thiene G. Arrhythmogenic right ventricular cardiomyopathy: diagnosis, prognosis, and treatment. *Heart* 2000; 83: 588-95.
2. Thiene G, Nava A, Corrado G, et al. Right ventricular cardiomyopathy and sudden death in young people. *N Eng J Med* 1988; 318: 129-33.
3. Danieli GA, Rampazzo A. Genetics of arrhythmogenic right ventricular cardiomyopathy. *Curr Opin Cardiol* 2002; 17: 218-21.
4. McKenna WJ, Thiene G, Nava A, et al. Diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy. Task Force of the Working Group Myocardial and Pericardial Disease of the European Society of Cardiology and of the Scientific Council on Cardiomyopathies of the International Society and Federation of Cardiology. *Br Heart J* 1994; 71: 215-8.
5. Davison AC, Hinkley DV. Bootstrap methods and their applications. *Cambridge University Press*, UK, 1997.

6. Pelliccia A, Maron BJ. Preparticipation cardiovascular evaluation of the competitive athlete: perspectives from the 30-year Italian experience. *Am J Cardiol* 1995; 75: 827-9.
7. Maron BJ. Sudden death in young athletes. *N Eng J Med* 2003; 359: 1064-75.
8. Corrado D, Pelliccia A, Bjornstad HH, et al. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J* 2005; 26: 516-24.
9. Pigozzi F, Spataro A, Fagnani F, et al. Preparticipation screening for the detection of cardiovascular abnormalities that may cause sudden death in competitive athletes. *Br J Sports Med* 2003; 37: 4-5.
10. Goldenberg I, Moss AJ, Maron BJ, et al. Cost-effectiveness of implanted defibrillators in young people with inherited cardiac arrhythmias. *Ann Noninvasive Electrocardiol* 2005; 10: 67-83.

Ocena ekonomiczna badań przesiewowych w kierunku rodzinnej postaci arytmogennej kardiomiopatii prawej komory w Polsce

Ewa Kowalik, Elżbieta K. Włodarska, Olgierd Woźniak, Piotr Hoffman

Klinika Wad Wrodzonych Serca, Instytut Kardiologii, Warszawa

Streszczenie

Wstęp: Arytmogenna kardiomiopatia prawej komory (ARVC) jest chorobą mięśnia sercowego, w której tkanka mięśnia prawej komory jest zastępowana tkanką tłuszczową oraz włóknistą, co powoduje niestabilność elektryczną oraz zaburzenia kurczliwości prawej komory. W obrazie klinicznym dominują komorowe zaburzenia rytmu serca (pierwszym objawem choroby może być nagły zgon), a u chorych z ciężkim uszkodzeniem mięśnia serca – objawy niewydolności prawokomorowej. Arytmogenna kardiomiopatia jest drugą, po kardiomiopatii przerostowej, przyczyną nagłego zgonu wśród sportowców i młodych, dotychczas zdrowych osób. Choroba jest uwarunkowana genetycznie przynajmniej w 50% przypadków.

Cel: Ocena kosztów oraz efektywności kosztowej badań przesiewowych w kierunku rodzinnej postaci kardiomiopatii w grupie bezobjawowych krewnych chorych z ARVC w Polsce.

Metodyka: W badaniu wzięło udział 239 osób (średni wiek 35 lat, 120 mężczyzn), dotychczas zdrowych, należących do 42 rodzin, w których stwierdzono ARVC. W analizie uwzględniono bezpośrednie koszty medyczne, tj. koszty wizyt ambulatoryjnych oraz dodatkowych badań diagnostycznych – spoczynkowy EKG, przezklatkowe badanie echokardiograficzne (TTE), badanie późnych potencjałów oraz rezonans magnetyczny (RMI) serca. Jako jednostkę efektywności w analizie ekonomicznej przyjęto wykrycie jednego przypadku rodzinnej postaci ARVC. Badanie zostało przeprowadzone z perspektywy płatnika usług medycznych.

Wyniki: U wszystkich osób wykonano spoczynkowy EKG oraz TTE. Następnie 35 osób z podejrzeniem ARVC zostało skierowanych na badanie RMI serca oraz późnych potencjałów. Ostatecznie kryteria diagnostyczne dla rozpoznania ARVC stwierdzono u 29 chorych, natomiast u kolejnych 57 osób stwierdzono graniczną postać choroby. Całkowite koszty badań przesiewowych w badanej populacji wyniosły 71 090 PLN. Koszt przeprowadzonych badań obrazowych wyniósł 51 970 PLN, w tym największy udział miały badania echokardiograficzne. Średni koszt wykrycia jednego przypadku rodzinnej postaci ARVC wyniósł 2451 PLN. Współczynnik koszty-efektywność dla wykrycia jednego przypadku ARVC lub formy granicznej choroby był natomiast znacznie niższy i wyniósł 827 PLN.

Wnioski: Koszty wczesnego wykrycia przypadków rodzinnej postaci ARVC w warunkach polskich są niskie. Dzięki możliwości wdrożenia prewencji pierwotnej nagłego zgonu sercowego badania przesiewowe w populacji bezobjawowych osób z wywiadem rodzinnym ARVC są postępowaniem kosztowo efektywnym.

Słowa kluczowe: kardiomiopatia, badania przesiewowe, efektywność kosztowa

Kardiol Pol 2007; 65: 1442–1446

Adres do korespondencji:

lek. med. Ewa Kowalik, Klinika Wad Wrodzonych Serca, Instytut Kardiologii, ul. Alpejska 42, 04-628 Warszawa, tel.: +48 22 343 42 63, e-mail: ewa.kowalik@gmail.com

Praca wpłynęła: 19.04.2007. **Zaakceptowana do druku:** 10.10.2007.