Ewa Agnieszka Świerżyńska-Wodarska

Zastosowanie i optymalizacja funkcji adaptacji częstotliwości rytmu w stymulatorach serca

Application and optimization of the rate response function in dual-chamber cardiac pacemakers

Rozprawa doktorska na stopień doktora
w dziedzinie nauk medycznych i nauk o zdrowiu
w dyscyplinie nauki o zdrowiu
przedkładana Radzie Dyscypliny Nauk o Zdrowiu
Warszawskiego Uniwersytetu Medycznego

Promotor: Prof. dr hab. n. med i n. o zdr. Renata Główczyńska

Warszawa, 2025

8. Abstract

Title: Application and optimisation of the rate response function in dual-chamber cardiac pacemakers

The use of pacemakers in the therapy of cardiological diseases has been known since the 1950s and is widely applied in Poland and around the world. [1] In Poland, approximately 30,000 pacemaker implantation procedures are performed annually. The percentage of pacemaker-dependent patients ranges from 2.2% to 7.2% and varies depending on the reason for implantation and the selected definition of pacemaker dependency. [2]

Implantable device manufacturers are constantly striving to develop increasingly advanced algorithms and parameters aimed at improving the therapeutic and diagnostic capabilities of cardiac implantable electronic devices. The ability to adjust the programmable pacing parameters for a specific patient based on their medical history and lifestyle contributes to improving well-being and enhancing the quality of life for patients. [3-4] Modern pacemakers are equipped with a function that adjusts the heart rate frequency to the patient's current needs (the "rate response" function). This function relies on various mechanisms, such as: a built-in accelerometer responding to increased chest movement (vibrations), algorithms detecting metabolic oxygen demand, intra-cardiac impedance analysis, patient rhythm analysis (QT interval), and combinations of these mechanisms. [5]

Article No. 1 extensively describes the technical aspects of the available sensors related to the pacing rate adaptation function, along with their advantages and limitations.

The "rate response" function is widely used in patients with pacemaker, but the current knowledge, research, evidences, and guidelines regarding the impact of this function in dual-chamber pacemakers on patients' physical performance with chronotropic incompetence is insufficient, and their results are often contradictory. [6,7] This need was highlighted in the 2013 European Society of Cardiology guidelines on cardiac pacing and resynchronization therapy: " While there is evidence of superiority of VVIR pacing, compared with VVI pacing, in improving quality of life and exercise capacity, improvements in exercise capacity with DDDR, compared with DDD, have been inconsistent." [8] This led to the decision to choose this topic for research in preparation for this doctoral dissertation.

In the 2021 guidelines, for DDDR pacing, only one recommendation can be found: "In patients who present chronotropic incompetence and have clear symptoms during exercise, DDD with rate-responsive pacing should be considered" with a class IIa indication, level of evidence B. [9] However, no recommendations were provided regarding rate response parameters and upper sensor pacing rates. In the case of single-chamber pacing in patients with persistent atrial fibrillation, pacing in VVIR mode is recommended, with a higher class of recommendation (class 1), but with the lowest level of evidence (C). [9]

Article No. 2 comprehensively comments on the lack of clinical research evidence on the application of cardiac implantable electronic devices, particularly the lack of studies on pacing modes, which in everyday clinical practice involves making decisions primarily based on experience.

In light of the above situation, before attempting to develop and verify an own method for selecting rate response settings, observations were made regarding the most commonly used rate response settings in a homogeneous group of patients with dual-chamber pacemakers from one manufacturer.

Article No. 3 presents the results of a retrospective observational study describing the most commonly used rate response settings in outpatient conditions at two academic centers. By analyzing demographic and clinical data of 200 patients, factors related to the use of specific pacing parameters were examined.

The rate response function was most frequently activated in patients with sick sinus syndrome (72.5%). In almost all groups, the predominant baseline pacing frequency setting was 60 beats per minute (bpm), the pacing frequency for daily activity-related exertion (ADL) was 85 bpm, and the upper rate response frequency (USR) was set to 110 bpm. The ADL, USR, and upper conduction rate (UTR) values were higher in patients with surgically corrected valve defects. The UTR varied between groups, ranging from 120 to 130 bpm. Functions limiting ventricular pacing before prolonging the atrioventricular interval were also most frequently activated in patients with sick sinus syndrome and those with a ventricular pacing frequency < 50%. An interesting observation was more frequent use of these functions in women.

The main conclusion from this analysis was the observation that rate response parameters are rarely adjusted to age, even though the maximum heart rate — used as a reference for exercise adjustment in cardiac rehabilitation and physical fitness assessment — is proportionally calculated based on age. Based on available knowledge and the described results, it was deemed appropriate for rate response parameters to be selected in a more detailed and individualized manner, taking into account the patient's age, comorbidities, lifestyle, and individual needs.

To verify this assumption, a prospective randomized crossover study was developed, in which physical performance in patients with dual-chamber pacemakers was assessed after activating several sets of rate response parameters.

Article No. 4 provides a detailed description of the prospective study protocol. Note — after the publication of this article, changes had to be made to the protocol. The duration of the observation between visits and the change of stimulation parameters was changed from 3 months to 7-14 days. In addition, the study assumptions were verified, and the minimum sample size required to achieve a statistically significant difference in the study results was recalculated. The target number of participants in recruitment was reduced. Approval was obtained from the Bioethics Committee for changes to the protocol. The company with which the contract for medical experiment liability insurance was signed was also informed of the change in the protocol.

Article No. 5 presents the results of the prospective study. Seventeen patients were enrolled in the study. At the time of inclusion, the average percentage of atrial pacing was 67%, and the average percentage of ventricular pacing was 54%. The average age of the patients was 70 years.

Comparing the results of an electrocardiographic treadmill exercise test with three different rate response settings showed a statistically significant difference in the exertion

level, expressed in MET units. In DDD mode, patients achieved an average of 9.5 (3.4) MET, while in DDDR mode with the settings described in the study protocol, they achieved 11.6 (3.1) MET ($p = 0.002$). Additionally, an improvement in the duration of the exercise phase of the electrocardiographic treadmill test was observed. In DDD mode, the average exercise time was 8.25 (4.1) minutes, while in DDDR mode, it was 10.3 (3.9) minutes ($p = 0.005$).

Comparing the results of the 6MWT did not show a statistically significant difference in the distance walked. In DDD mode, the average distance was 443 (98) meters, while in DDDR mode, it was 455 (63) meters ($p = 0.472$). However, a statistically significant reduction in reported fatigue on the Borg scale was observed during tests conducted in DDDR mode [3 (0) vs. 4 (1), $p = 0.002$].

In addition to the exercise tests, the results of the questionnaire-based surveys were compared. In relation to quality of life assessment using the SF-36 questionnaire, a statistically significant but small difference was observed in favor of the DDDR mode (94 vs. 88 points, $p = 0.046$).

The rate response function, with maximum pacing frequency parameters set according to the maximum heart rate predicted for the patient's age, allows for improved exercise tolerance in patients with dual-chamber pacemakers and predominant atrial pacing. It is recommended to individually adjust sensitivity, intensity of response, and limits related to rate response parameters in patients with limited exercise tolerance.

The dissertation emphasizes the importance of personalizing rate response parameters in pacemakers, pointing out the need for further research to develop standards and optimal strategies for programming these functions, which improve the treatment outcomes of patients with implanted devices.