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CASE REPORT
Medical management of arrhythmias

Antiarrhythmic effects of baroreceptor activation therapy in chronic heart failure: a case report

Dong Wang *, Christian Veltmann, Johann Bauersachs, and David Duncker

Department of Cardiology and Angiology, Hannover Medical School, Carl-Neuberg-Straße 1, 30625 Hannover, Germany

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Background Autonomic imbalance represents a keystone of chronic heart failure (HF) with substantial clinical and prognostic implications. Baroreceptor activation therapy (BAT) is a new therapeutic strategy to target the autonomic dysbalance by electrical stimulation of carotid baroreceptors. Besides its known beneficial effects on HF parameters, BAT is also supposed to trigger potential antiarrhythmic effects, which may additionally contribute to HF improvement.

Case summary We report on a 70-year-old male with progredient shortness of breath and advanced HF in the context of an extensive cardiovascular history. After optimization of pharmacologic and device-related therapy, the decision was made to implant a BAT system (Barostim Neo, CVRx) to improve functional cardiac parameters and support symptomatic improvement. Implantation was associated with an overall clinical improvement assessed during outpatient visits every 6 months. Frequency of ventricular arrhythmic events declined, and atrial fibrillation ceased spontaneously. Echocardiography revealed an amelioration in left ventricular systolic function. Numbers of HF hospitalization decreased after Barostim implantation.

Discussion We present a patient with an extensive cardiovascular history and fully exploited pharmacologic and device-related therapy, who showed improvement in New York Heart Association (NYHA) functional classification, left ventricular systolic function, and reduction of arrhythmic events following implantation of the BAT device. This case presents an additional positive potential of BAT for HF patients in terms of reduction of arrhythmia burden. These results should be confirmed by further clinical trials.

Keywords Arrhythmias • Atrial fibrillation • Baroreceptor activation therapy • BAT • Heart failure • Case report

ESC curriculum 5.3 Atrial fibrillation • 6.2 Heart failure with reduced ejection fraction • 6.1 Symptoms and signs of heart failure

Learning points

- Autonomic imbalance is a key feature of heart failure and represents a treatment target.
- Baroreceptor activation therapy targets autonomic imbalance and improves heart failure symptoms and reduces arrhythmia events.

Introduction

Heart failure (HF) remains a highly prevalent global epidemic associated with considerable morbidity, mortality, and health loss burden, particularly in the aged population.[1] Regardless of the aetiology, autonomic imbalance characterized by disturbed mechanisms of parasympathetic and sympathetic vasoactive control represents a major trigger for HF symptoms resulting in a plethora of clinical and prognostic implications.[2] A new therapeutic strategy is to target the autonomic dysbalance by electrical stimulation of carotid baroreceptors and thereby enhance parasympathetic output.[3] Baroreceptor activation therapy (BAT) was initially developed to treat drug-resistant hypertension and has recently shown to be an effective treatment option for patients with HF.[4] Baroreceptor activation therapy significantly improves

* Corresponding author. Tel: +49 511 5320, Email: Wang.Dong@mh-hannover.de
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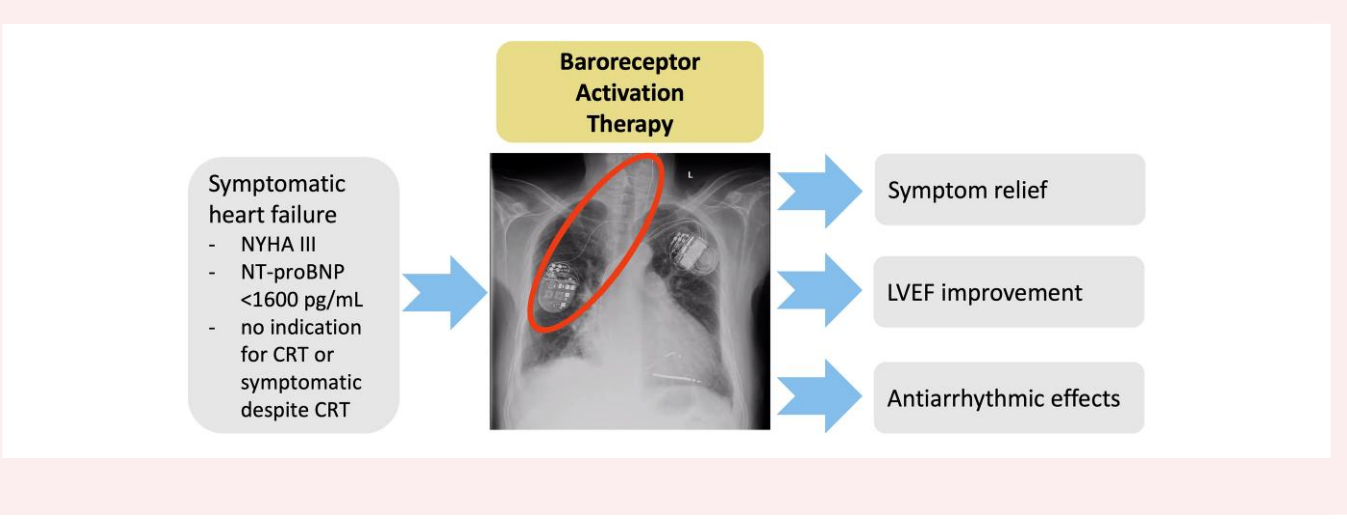
ejection fraction, plasma biomarkers, health care resource use, functional capacity, New York Heart Association (NYHA) functional class, and quality of life.[4–6] However, the effect of BAT on arrhythmia has not been studied before.

We herein report on a patient with an extensive cardiovascular history, undergoing successful BAT. In this patient, BAT led to decline of arrhythmic events and cessation of atrial fibrillation (AF), which contribute to HF improvement.

Summary figure



Case presentation

The patient was a 70-year-old male, who presented with reduced physical resilience and progredient shortness of breath, corresponding to NYHA functional class III. He had a baseline blood pressure of 112/59 mmHg, heart rate of 60 b.p.m, and advanced HF in the context of ischaemic cardiomyopathy and an extensive cardiovascular history.

His cardiovascular risk factors included insulin-dependent diabetes mellitus type 2 since the age of 31, arterial hypertension, hyperlipidaemia, and a smoking history with 50 pack years. Other comorbidities were diabetic nephropathy, thyroid nodules, and peripheral arterial disease, which had undergone endarterectomy and patch-plastic surgery. His current medication consisted of bisoprolol 5 mg b.i.d., phenprocoumon q.d., ramipril 5 mg b.i.d., eplerenone 25 mg q.d., digoxin 0.2 mg q.d., torasemide 10 mg t.i.d., simvastatin 40 mg q.d., allopurinol 150 mg q.d., and insulin. Physical examination revealed no abnormalities apart from leg oedema. Echocardiography showed a reduced left ventricular ejection fraction (LVEF) of 31%. Laboratory tests revealed an elevated NT-proBNP level and reduced kidney function, corresponding to stage 3A of chronic kidney disease.

His cardiovascular history started with a silent anterior myocardial infarction back at the age of 50 years. A later cardiac catheter examination revealed a three-vessel coronary artery disease with high-grade stenosis of the right coronary artery (RCA) leading to percutaneous coronary interventions (PCI) of the RCA. Over the following years, the RCA has been intervened with stent implantation three times. At the age of 65, the patient underwent implantation of a cardiac resynchronization therapy defibrillator (CRT-D) device due to symptomatic HF, severely reduced LV function, and a masked left anterior hemiblock with existing right bundle branch block and first-degree atrioventricular (AV) block. Only 1 month later, he suffered a non-ST-elevation myocardial infarction (NSTEMI) accompanied by slow ventricular tachycardia (VT) and several episodes of paroxysmal atrial flutter and AF. This was followed by a 4-year episode of multiple and frequent hospitalizations due to cardiac decompensations. During this time, an external cardioversion and catheter ablation of atrial flutter were performed. Atrial fibrillation had become persistent at this point of time, and the first-degree AV block progressed to third-degree AV block. The patient was reluctant to undergo further interventional procedures and refused pulmonary vein isolation.

Despite maximum pharmacologic and CRT-D device therapy and given the patients' ever deteriorating medical condition with recurring episodes of HF decompensation and arrhythmia events (see *Table 1*), the decision was made to implant a BAT system (Barostim Neo, CVRx, Inc. of Minneapolis, MN, USA). In brief, a small incision was made in the neck and the carotid artery bifurcation with baroreceptors exposed. The electrode is sutured on the bifurcation and connected with a pulse generator, which is implanted in an infraclavicular subcutaneous chest wall pocket. Baroreceptor activation therapy stimulation was carried out with a frequency of 60 pulse per second (pps) and an impulse strength of 8 mA. The surgery proved uneventful, with no intraoperative adverse events nor post-operative complaints of discomfort encountered. The patient was discharged 5 days post-operation with no modification of medication. The post-operative *situs* is depicted in *Figure 1*.

Over the following months, the NYHA functional class improved from class III to class II. Comparison of pre- to post-echocardiographic investigations revealed an amelioration in LV systolic function (post) as compared with a severely compromised LV before implantation (see Supplementary material online, *Video S1*) accompanied by a moderate improvement in LVEF to 33%. Of particular note, the overall atrial tachycardia (AT)/AF burden decreased markedly. Frequency of ventricular arrhythmic events also showed a decrease in the occurrence of sustained and non-sustained VT events (*Table 1*).

Fourteen months post-implantation of the BAT system, AF—which had been previously assessed being persistent—then ceased spontaneously (*Figure 2*). Electrocardiogram recorded in paused BAT device mode showed no AF events, whereas in active mode, the Barostim system exhibited the typical artefacts (*Figure 3*). At the age of 72, the patient suffered another NSTEMI, which led to deterioration of cardiac function and overall condition. Nine months later, the patient died at the age of 73 due to HF and multiorgan failure.

Discussion

Autonomic imbalance is a common finding in heart failure with reduced ejection fraction patients, and cardiac autonomic modulation by the use

Table 1 Arrhythmia events recorded by the cardiac resynchronization therapy defibrillator device

Year	AF burden (%)	Non-sustained VT	Sustained VT
5 years before BAT	8.7	0	6
4 years before BAT	50.6	2	0
3 years before BAT	59.6	0	0
2 years before BAT	1.5	0	0
1 year before BAT	49.6	6	2
BAT	100	0	0
1 year after BAT	100	0	0
2 years after BAT	12.1	2	0
3 years after BAT	<0.1	0	0

Atrial fibrillation burden and frequency of ventricular arrhythmic events over an 8-year period.
BAT, baroreceptor activation therapy; AF, atrial fibrillation; VT, ventricular tachycardia.

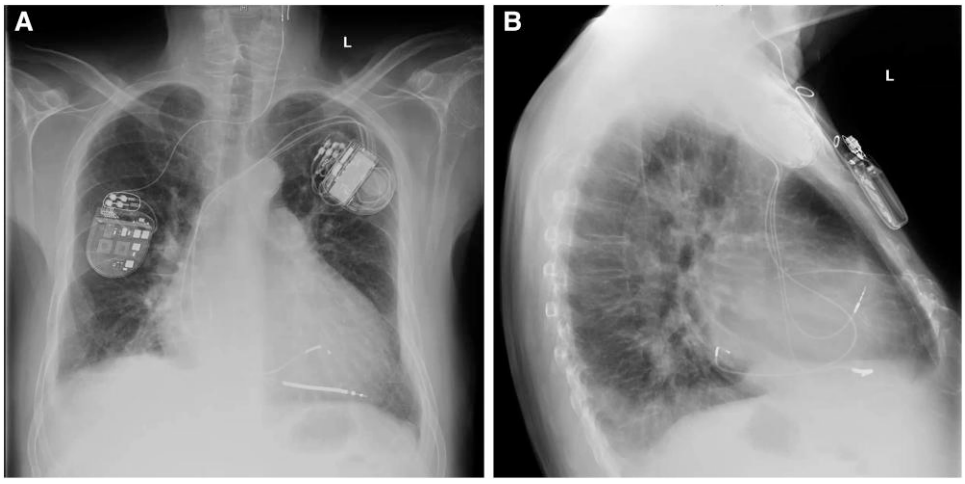


Figure 1 Chest X-ray from the front (*A*) and lateral (*B*) depicting the baroreflex activation therapy device (right chest) and the cardiac resynchronization therapy defibrillator (left chest) in the frontal recording (*A*).

of carotid BAT has yielded favourable results.[5,6] Beside improving cardiac function, exercise capacity, and reducing hospitalization, we present antiarrhythmic effects by BAT in this case report.

In our patient, arrhythmia events were constantly monitored by the CRT-D device after implantation. Before initiation of BAT, the patient suffered one episode of slow VT in the context of an NSTEMI, eight episodes of VT treated by the CRT-D device, and eight episodes of non-sustained VTs. This number dropped after implantation of BAT. After initiation of BAT, only two short episodes of non-sustained VTs occurred.

On a supraventricular level following diagnosis of paroxysmal AF at the age of 65, it progressed to persistent AF 4 years later. Multiple medical and interventional treatments were not able to reach sustained rhythm control. However, 14 months after BAT, AF spontaneously converted into sinus rhythms. Sinus rhythm remained until the patient deceased.

The physiological purpose of the baroreceptor reflex is to provide sufficient blood flow to the brain after postural change. It is a negative feedback loop in which an elevated blood pressure causes the heart rate to decrease. Decreased blood pressure decreases baroreflex activation and causes heart rate to increase and to retain sufficient blood flow. Exogenous electrical stimulation of the baroreflex leads to a decrease in heart rate in conscious resting normal dogs.[7] In healthy human probands, electrical stimulation of the carotid baroreflex can prolong the R-R interval secondary to augmented parasympathetic activity.[8]

The antiarrhythmic potential of baroreceptor stimulation was first described in preclinical trials. Baroreceptor activation therapy effectively increases the threshold for lethal ventricular arrhythmias in dogs with chronic HF.[9] In addition, it suppresses electrically or mechanically induced AF by suppressing rapid firing and inhibiting the intrinsic cardiac autonomic system.[10] Baroreceptor activation therapy causes a progressive increase in AF threshold, prolongs atrial effective refractory period (AERP), and shortens the window of vulnerability, thereby contributing to an antiarrhythmic effect.[10]

Current clinical data hint at the antiarrhythmic potential of BAT therapy. A case report by Robles-Mezcua *et al.*[11] described a patient exhibiting reduced ventricular arrhythmias and AF following BAT implantation. In a randomized clinical trial by Zile *et al.*,[6] a relative reduction of 50% in cardiac arrhythmic events was observed in the BAT

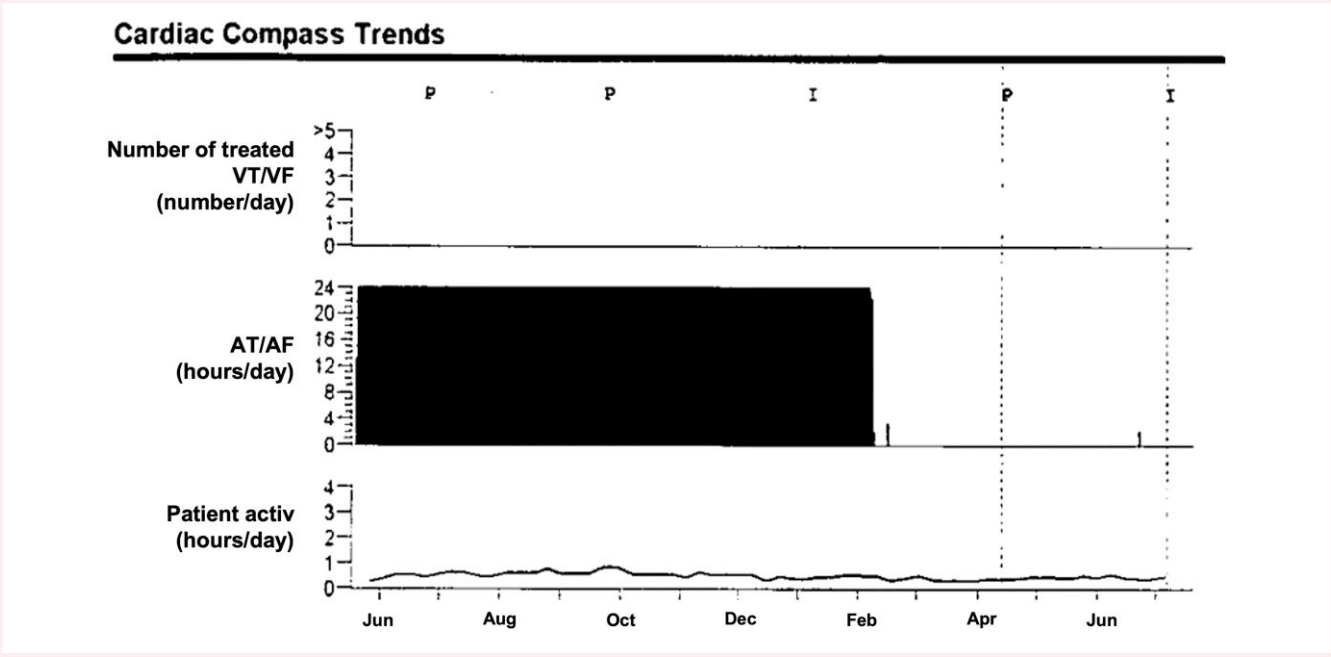


Figure 2 Cardiac resynchronization therapy defibrillator interrogation between 5 and 19 months after baroreceptor activation therapy including ventricular tachycardia/ventricular fibrillation episodes per day (top), atrial fibrillation burden (hours/day; middle), and patient activity per day (bottom). AF, atrial fibrillation; AT, atrial tachycardia; VT, ventricular tachycardia; VF, ventricular fibrillation.

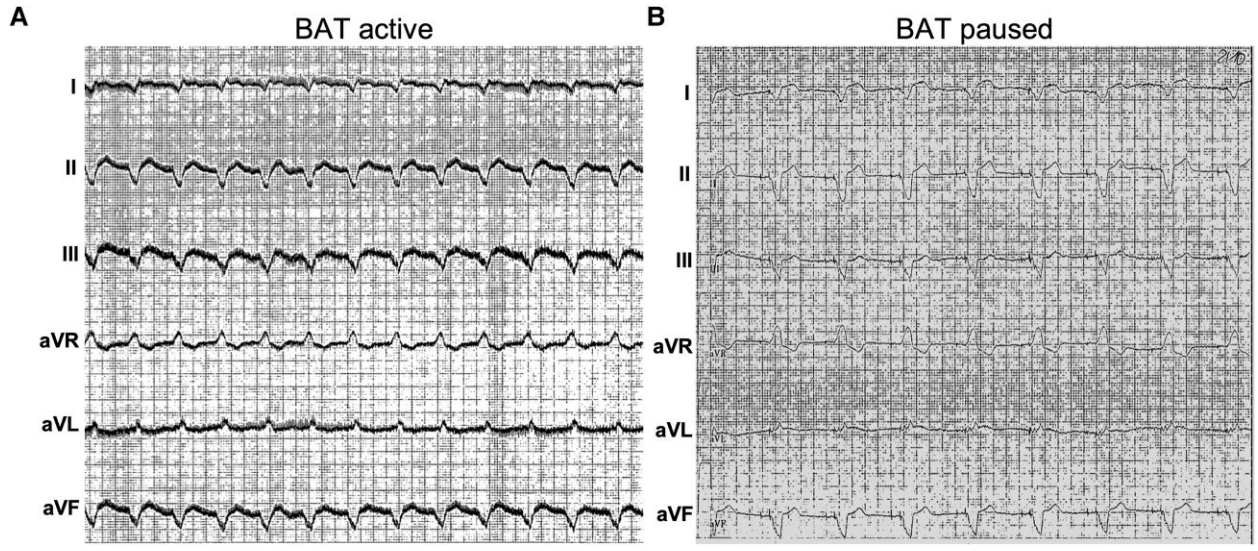


Figure 3 Electrocardiogram 19 months after baroreceptor activation therapy after spontaneous conversion of atrial fibrillation. (*A*) In active baroreceptor activation therapy mode, the electrocardiogram records typical artefacts not interfering in the pacing by the cardiac resynchronization therapy defibrillator device. (*B*) The baroreceptor activation therapy system in paused mode, showing no atrial fibrillation. BAT, baroreceptor activation therapy.

group. Although not reaching statistical significance, a clear trend towards improvement was observed.[6] This can be seen as a starting point for future investigations, particularly, as AF is known to be associated with more marked autonomic dysfunction and lower therapeutic benefit from either beta-blockade or CRT compared with patients in sinus rhythm.[12]

Currently, the indications for BAT are patients who remain symptomatic despite treatment with guideline-directed medical therapy,

are NYHA class III or class II (who had a recent history of class III), have an LVEF ≤35%, an NT-proBNP <1600 pg/mL, and have no indication for CRT or remain symptomatic despite CRT. Contraindications include (i) overt cranial location of the bilateral carotid bifurcation (above the mandible), (ii) carotid stenosis >50%, (iii) ulcerative plaques in the carotid artery, (iv) baroreflex failure or autonomic neuropathy, and (v) uncontrolled, symptomatic cardiac bradyarrhythmias.[4]

In the 2021 ESC and 2022 AHA guidelines for HF, BAT was described to offer a modest improvement in effort capacity and quality of life.[13,14] However, the evidence was considered insufficient to support specific guideline recommendations as no mortality or hospitalization rate results were available, yet. To close these gaps, the BeAT-HF study, a multicentre, prospective, randomized controlled trial was conducted. This study was completed at the beginning of 2023, and the final detailed results will be awaited by the end of 2023 and will provide valuable insights into the efficacy of BAT and the treatment of patients with HF.[15]

In conclusion, BAT is a promising therapeutic option for patients with advanced HF to improve NYHA classification, EF, and reduce number of hospitalizations. In addition, it possesses antiarrhythmic effects that could further contribute to HF improvement.

Lead author biography

Dr Dong Wang obtained his medical degree from the University of Hamburg, Germany, and underwent his postdoctoral training at the University of California, San Francisco, USA. He specializes in cardiology at the Medical School Hannover, Germany, and has a special interest in heart failure, electrophysiology, and rhythmology.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: D.W. does not have any conflicts of interest to declare. C.V. received modest honorary for lectures and consultant activities from Abbott, Biotronik, and Medtronic. J.B. received honoraria for lectures/consulting from Novartis, Vifor, Bayer, Pfizer, Boehringer Ingelheim, AstraZeneca, Cardior, CVRx, BMS, Amgen, Corvia, Norgine, Edwards, and Roche, not related to this article, and research support for the department from Zoll, CVRx, Abiomed, Norgine, and Roche, not related to this article. D.D. received modest lecture honorary, travel grants, and/or a fellowship grant from Abbott, AstraZeneca, Biotronik, Boehringer Ingelheim, Boston Scientific, CVRx, Medtronic, Microport, Pfizer, and Zoll.

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Data availability

The data underlying this article are available within the article and in its online Supplementary material.

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