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Eligibility for Baroreflex Activation Therapy and medication adherence in patients with apparently resistant hypertension

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Abstract

Uncontrolled hypertension is a main risk factor for cardiovascular morbidity. Baroreflex activation therapy (BAT) is an effective therapy option addressing true resistant hypertension. We evaluated patients' eligibility for BAT in a staged assessment as well as adherence to antihypertensive drug therapy. Therefore, we analyzed files of 345 patients, attending the hypertension clinic at University Medicine Göttingen. Additionally, gas chromatographic-mass spectrometric urine analyses of selected individuals were performed evaluating their adherence. Most common cause for a revoked BAT recommendation was blood pressure (BP) control by drug adjustment (54.2%). Second leading cause was presence of secondary hypertension (31.6%). Patients to whom BAT was recommended (59 (17.1%)) were significantly more often male (67.8% vs. 43.3%, $P = .0063$), had a higher body mass index (31.8 ± 5.8 vs. 30.0 ± 5.7 kg/m², $P = .0436$), a higher systolic office (168.7 ± 24.7 vs. 147.7 ± 24.1 mmHg, $P < .0001$), and 24h ambulatory BP (155.0 ± 14.6 vs. 144.4 ± 16.8 mmHg, $P = .0031$), took more antihypertensive drugs (5.8 ± 1.3 vs. 4.4 ± 1.4, $P < .0001$), and suffered more often from numerous concomitant diseases. Eventually, 27 (7.8%) received a BAT system. In the toxicological analysis of 75 patients, mean adherence was 75.1%. 16 patients (21.3%) showed non-adherence. Thus, only a small number of patients eventually received a BAT system, as treatable reasons for apparently resistant hypertension could be identified frequently. This study is—to our knowledge—the first report of a staged assessment of patients' suitability for BAT and underlines the need for a careful examination and indication. Non-adherence was proven to be a relevant issue concerning apparently resistant hypertension and therefore non-eligibility for interventional antihypertensive therapy.

1 | INTRODUCTION

Uncontrolled hypertension and resistant hypertension are common health care problems. Prevalence differs due to study designs and definitions, but is estimated around 10%-30% of hypertensive patients.[1-5] *Resistant hypertension* is defined as insufficient blood pressure (BP) control ≥140/90 mmHg despite the intake of ≥3 antihypertensive drugs including a diuretic.[6-8] *Uncontrolled or apparently resistant hypertension* furthermore includes the lack of BP control due to inadequate treatment adjustment or poor adherence among other factors.[6]

Lifestyle modification and drug therapy are the fundamental cornerstones of antihypertensive treatment.[7,8] Nevertheless, previous studies have underlined the widely divergent rates of medication adherence in patients with hypertension, with non-adherence rates from 3.3% to 86.1%.[9,10] In addition, Patel et al showed non-adherence to be an important reason for classifying patients as non-eligible for receiving further treatment options for uncontrolled hypertension such as interventional therapies.[11]

As uncontrolled hypertension is one of the main risk factors of cardiovascular diseases such as myocardial infarction, heart failure, and stroke, causing high morbidity and mortality as well as huge health care costs,[12-17] we evaluated patients' treatment adherence and other causes of apparently resistant hypertension in our baroreflex activation therapy (BAT) clinic.

As drug therapy alone is sometimes insufficient for BP adjustment, device-based treatment options can be considered.[8] BAT is one therapy option addressing true resistant hypertension and was recommended within the ESH guidelines 2013.[18-20] Stimulating baroreceptors on the carotid glomus, BAT triggers the reduction in BP by activating vegetative feedback loops resulting in an inhibition of the sympathetic nervous system.[21]

As discussed elsewhere, BAT is an efficient and safe treatment option to achieve BP control in individuals with true therapy-resistant hypertension and has further beneficial effects on the renal and vascular system.[22-28] After BAT implantation, a significant reduction in both office and ambulatory systolic blood pressure (SBP) and diastolic blood pressure (DBP) could be documented, accompanied by a relevant reduction in prescribed antihypertensive drugs.[22,23] Described potential side effects are, for example, indisposition with device components, wound complications, and hematoma.[29] A thorough evaluation must therefore be carried out prior to a BAT. We analyzed patients' suitability for this treatment option and reasons for non-eligibility in patients with apparently resistant hypertension.

2 | MATERIAL AND METHODS

2.1 | Study design, population characteristics, and ethical vote

In this retrospective monocentric study, we analyzed files and electronic health records of 345 patients with apparently resistant hypertension. Included patients visited the certified hypertension clinic of the University Medical Centre Göttingen from January 1, 2012, to December 31, 2019. Evaluated parameters were gender, age, body mass index (BMI), office and ambulatory BP, type and number of antihypertensive drugs, history of smoking and pre-existing diseases such as chronic kidney disease (CKD), hyperlipoproteinemia (HLP), diabetes mellitus (DM), heart failure (HF), coronary heart disease (CHD), peripheral arterial disease (PAD), and stroke. The study was approved by the local ethics committee (# 29/2/19).

2.2 | BP measurement and verification of treatment eligibility

For office BP measurement, the initial BP reading was performed on both upper arms. The arm with the higher value was used for all following measurements. Subsequently, BP was measured twice within a 3-minute interval using a semiautomatic oscillometric device after 10 minutes of patient's rest. The results of the two readings were averaged.

24h ambulatory BP (ABP) was analyzed using an oscillometric Spacelabs recorder with measurements every 15 minutes during daytime and every 30 minutes at night. Readings were averaged after 24 hours.

Generally, a recommendation for BAT evaluation is given if the patient suffers uncontrolled BP despite the intake of at least 3 antihypertensive drugs in full dose after exclusion or treatment of secondary hypertension (sHTN). According to the 2013 ESH/ESC guidelines, when sHTN was suggested by medical history or examination, patients were screened for secondary reasons of hypertension such as renal artery stenosis (by renal duplex Doppler ultrasonography), hyperaldosteronism (by aldosterone-renin ratio), sleep apnea (by questionnaire of the federal association of sleep apnea Germany), and pheochromocytoma (by plasma-free metanephrines).[18] In case of suspected non-adherence, selective adherence tests were performed. Usually at least partial adherence (see below) was required for getting a recommendation for interventional therapy. Sufficient BP control was defined as BP <140/90 mmHg or the achievement of individual BP target following the 2013 ESH/ESC guidelines.[18]

2.3 | Detection of adherence

Additionally, in the period from January 1, 2014, to December 12, 2019, patients' adherence to antihypertensive medication was measured by direct biochemical urine analysis (gas chromatography-mass spectrometry (GC-MS)). The analyses were performed by the toxicological laboratory of the University Medical Centre Göttingen. Traceable substances were Clonidine, Moxonidine (in a high concentration), Doxazosin, Urapidil, Enalapril, Ramipril, Perindopril, Canrenone, Eplerenone, Spironolactone, Aliskiren, Irbesartan, Losartan, Valsartan, Bisoprolol, Metoprolol, Atenolol, Amlodipine, Lercanidipine, Nitrendipine, Nifedipine, Verapamil, Minoxidil, Amiloride, Hydrochlorothiazide, Furosemide, Torasemide, Indapamide, Piretanide, Xipamide, and Chlortalidone. Lisinopril, Candesartan,

TABLE 1 Baseline characteristics

	All patients (n = 345)	Patients with sHTN (n = 120)	Medicinally adjusted patients (n = 168)	Patients with recommendation for BAT (n = 59)	Patients getting a BAT implantation (n = 27)
Gender male/female (n)	178/167	69/51	78/90	40/19	18/9
Age (years)	62.2 ± 13.4	60.8 ± 12.5	63.8 ± 14.2	62.9 ± 10.6	57.5 ± 10.0
BMI (kg/m²)	30.3 ± 5.8	31.4 ± 6.1	29.5 ± 5.5	31.8 ± 5.8	31.8 ± 6.6
Office SBP (mmHg)	151.3 ± 25.4	159.3 ± 26.1	141.6 ± 20.8	168.7 ± 24.7	174.0 ± 27.6
Office DBP (mmHg)	84.9 ± 16.6	89.4 ± 18.0	80.4 ± 13.7	87.4 ± 18.6	94.3 ± 20.4
24h systolic ABP (mmHg)	146.6 ± 16.9	148.9 ± 17.2	140.1 ± 15.1	155.0 ± 14.6	155.8 ± 12.3
24h diastolic ABP (mmHg)	81.5 ± 12.6	83.8 ± 11.8	78.4 ± 12.7	80.8 ± 11.9	84.5 ± 13.6
Amount of antihypertensive drugs	4.7 ± 1.5	4.9 ± 1.5	4.2 ± 1.2	5.8 ± 1.3	6.2 ± 1.1
CKD	151 (43.8)	45 (37.5)	79 (47.0)	35 (59.3)	15 (55.6)
HLP	183 (53.0)	66 (55.0)	77 (45.8)	47 (79.7)	22 (81.5)
DM	112 (32.5)	40 (33.3)	45 (26.8)	34 (57.6)	12 (44.4)
HF	43 (12.5)	17 (14.2)	22 (13.1)	8 (13.6)	2 (7.4)
CHD	65 (18.8)	17 (14.2)	32 (19.0)	16 (27.1)	7 (25.9)
PAD	16 (4.6)	5 (4.2)	2 (1.2)	8 (13.6)	2 (7.4)
Stroke	20 (5.8)	7 (5.8)	7 (4.2)	7 (11.9)	1 (3.7)
History of smoking	52 (15.1)	19 (15.8)	24 (14.3)	10 (16.9)	6 (22.2)

Note: Results are expressed as mean±SD and number (%) respectively.

Abbreviations: ABP, ambulatory blood pressure; BMI, body mass index; CHD, coronary heart disease; CKD, chronic kidney disease; DBP, diastolic blood pressure; DM, diabetes mellitus; HF, heart failure; HLP, hyperlipoproteinemia; PAD, peripheral arterial disease; SBP, systolic blood pressure.

or Telmisartan were not traceable. Mean adherence was defined as the ratio of detected to traceable antihypertensive drugs. Complete adherence was defined as 100% proof of detectable medication, partial adherence or partial non-adherence as ≥66 but <100% and <66 but >0% evidence of medication intake respectively, and complete non-adherence was defined as no detection of any traceable antihypertensive medication.

2.4 | Statistics

Data analysis was performed using the statistical software GraphPad Prism 5 and Microsoft Excel 2010. The D´Agostino and Pearson omnibus normality test was used to test data for normal distribution. Differences in the investigated variables between different patient groups were analyzed using the unpaired t test or Mann-Whitney test. Results are expressed as mean value SD± or as respective percentages. The threshold for statistical significance was defined as P <.05.

3 | RESULTS

3.1 | Population characteristics

We examined 345 patients referred to the hypertension clinic for apparently resistant hypertension between January 1, 2012, and December 12, 2019. At their initial visit to our clinic, patients took 4.7 ± 1.5 antihypertensive drugs on average, most commonly diuretics, calcium channel antagonists, and beta blockers followed by renin-angiotensin-aldosterone system blockers and sympathicolytics. So, the definition of resistant hypertension, as uncontrolled BP despite the intake of ≥3 antihypertensive drugs including a diuretic, was initially fulfilled by 282 individuals. Patients' mean office SBP and DBP were 151.3 ± 25.4 mmHg and 84.9 ± 16.6 mmHg respectively. Mean 24h SBP was 146.6 ± 16.9 mmHg, and average 24h DBP was 81.5 ± 12.6 mmHg. Patients' mean age was 62.2 ± 13.4 years. More than half of patients suffered a concomitant disease such as obesity, CKD, HLP, DM, HF, CHD, PAD, or stroke. Tables 1 and 2 provide more detailed information on patients' baseline characteristics and primary medication.

3.2 | Eligibility for BAT and reasons for revoked treatment recommendation

Based on a screening for sHTN, 120 patients (34.8%) with varying underlying causes for sHTN were identified: 69 patients (20.0%) suffering from sleep apnea, 60 patients (17.4%) with hyperaldosteronism, 8 patients (2.3%) with renal artery stenosis, and 5 patients (1.4%) with suspected pheochromocytoma.

In the patient group without sHTN (n = 225), sufficient hypertension control could be achieved by drug adjustment in 168 patients (48.7% of all patients or rather 74.7% of the patients without sHTN). 8 patients (2.3%) could not be classified due to missing

follow-up data. In 49 patients (14.2%), sufficient BP control could not be achieved despite drug adjustment. In this subgroup, 10 patients (2.9%) showed non-adherence to the prescribed drug regimen, one patient received renal denervation, and one patient suffered from white coat hypertension (0.3% respectively). Ultimately BAT implantation was recommended to 37 patients in this group with insufficient hypertension control. BAT was also advised to 22 patients with uncontrolled sHTN. Of the 59 patients (17.1%) to whom a BAT system was recommended, 27 (7.8% of all patients and 45.8% of those it was recommended to) eventually received a BAT system as of analysis end. For 22 patients (6.4%), BAT evaluation was still ongoing or follow-up data was missing. One patient dropped out due to a carotid stenosis (0.3%), nine patients refused a BAT implantation (2.6%). A flowchart of suitability-assessment is shown in Figure 1.

Ultimately successful adjustment of pharmacologic antihypertensive treatment was the most common reason for a revoked recommendation of BAT implantation (54.2%). sHTN was the second leading cause (31.6%). Figure 2 shows the detailed presentation.

3.3 | Characteristics of eligible patients

Patients to whom BAT was recommended were significantly more often male (67.8% vs. 43.3%, P =.0063) and also had a significantly higher BMI (31.8 ± 5.8 vs. 30.0 ± 5.7 kg/m², P =.0436) than patients without advice for BAT. Documented systolic office (168.7 ± 24.7 vs. 147.7 ± 24.1 mmHg, P <.0001) and ambulatory BP (155.0 ± 4.6 vs. 144.4 ± 16.8 mmHg, P =.0031) were also higher. The average number of antihypertensive drugs was higher (5.8 ± 1.3 vs. 4.4 ± 1.4, P <.0001) in patients with a recommendation for BAT as well.

Concomitant diseases including CKD (59.3% vs. 43.8%), HLP (79.7% vs. 53%), DM (57.6% vs. 32.5%), PAD (13.6% vs. 4.6%), and stroke (11.9% vs. 5.85%) occurred significantly more often in people with recommendation for BAT (P =.0083 for CKD, <0.0001 for HLP and DM, 0.0004 for PAD, and 0.0289 for stroke, see Table 3). No significant differences could be seen concerning age, diastolic office, and ambulatory BP, HF, CHD, and smoking.

TABLE 2 Primary antihypertensive medication over all patients

Type of antihypertensive drug	Number of patients (%)
ACE inhibitor	147 (42.6)
AT1 antagonist	185 (53.6)
Beta blocker	277 (80.3)
Calcium channel antagonist	267 (77.4)
Diuretics	282 (81.7)
Aldosterone antagonist	67 (19.4)
Alpha blocker	89 (25.8)
Sympathicolytics	160 (46.4)
Vasodilators	69 (20.0)
Renin inhibitors	18 (5.2)

Note: Results are expressed as number (%).

3.4 | Medication adherence

Patients' medication adherence was measured in 75 individuals. 59 (78.7%) showed adherence to ≥66% of the prescribed drug regimes, including 41 patients (54.7%) with complete adherence. 16 patients (21.3%) showed non-adherence, with 9 patients (12.0%) exhibiting partial and 7 patients (9.3%) showing complete non-adherence.

Mean adherence over all patients was 75.1%. Patients with adequate BP control under medication (mainly <140/90 mmHg) exhibited the best mean adherence with 89.3%. Furthermore, patients to whom BAT was recommended or who received a BAT system showed an above-average adherence (87.4 and 86.6%, respectively). Table 4 provides the detailed adherence analysis.

4 | DISCUSSION

Uncontrolled hypertension is one of the main risk factors for cardiovascular morbidity and mortality.[12-17] We evaluated reasons for apparently resistant hypertension in patients visiting our BAT clinic.

Data were acquired retrospectively from a single-center analysis, imposing some limitations on our investigation. Despite this limitation, this study is the first to describe the results of a standardized BAT evaluation in one of the largest BAT centers. Concerning patients' characteristics, our study collective was comparable with other collectives with resistant hypertension,[3,5] with patients suffering from numerous comorbidities such as obesity, DM, dyslipoproteinemia, CHD, and CKD.

In the treatment of hypertension, lifestyle modification and drug therapy are the fundamental cornerstones for reaching BP control.[7,8] Despite optimal medication, BP sometimes remains above the desired threshold. In this case, interventional therapies such as baroreflex activation or renal denervation can be used to reach BP control.[8,20]

BAT is a treatment option that leads to efficient BP reduction in individuals with therapy-resistant hypertension.[22-24] Described potential side effects are, for example, indisposition with device components causing globus sensation, pain, or voice problems as well as wound complications.[29,30] Therefore, when selecting suitable patients, a structured evaluation should accompany the risk/benefit analysis. In a recent 2-year follow-up after BAT implantation, a significant reduction in office and ambulatory BP was documented.[23] Furthermore, additional positive effects of BAT could be verified, that is, reduction in proteinuria, aortic pulse pressure, augmentation index, and pulse wave velocity.[26-28]

These additional effects are of particular importance since patients with resistant hypertension frequently suffer from various comorbidities such as CKD, which highly increase their risk of cardiovascular diseases.

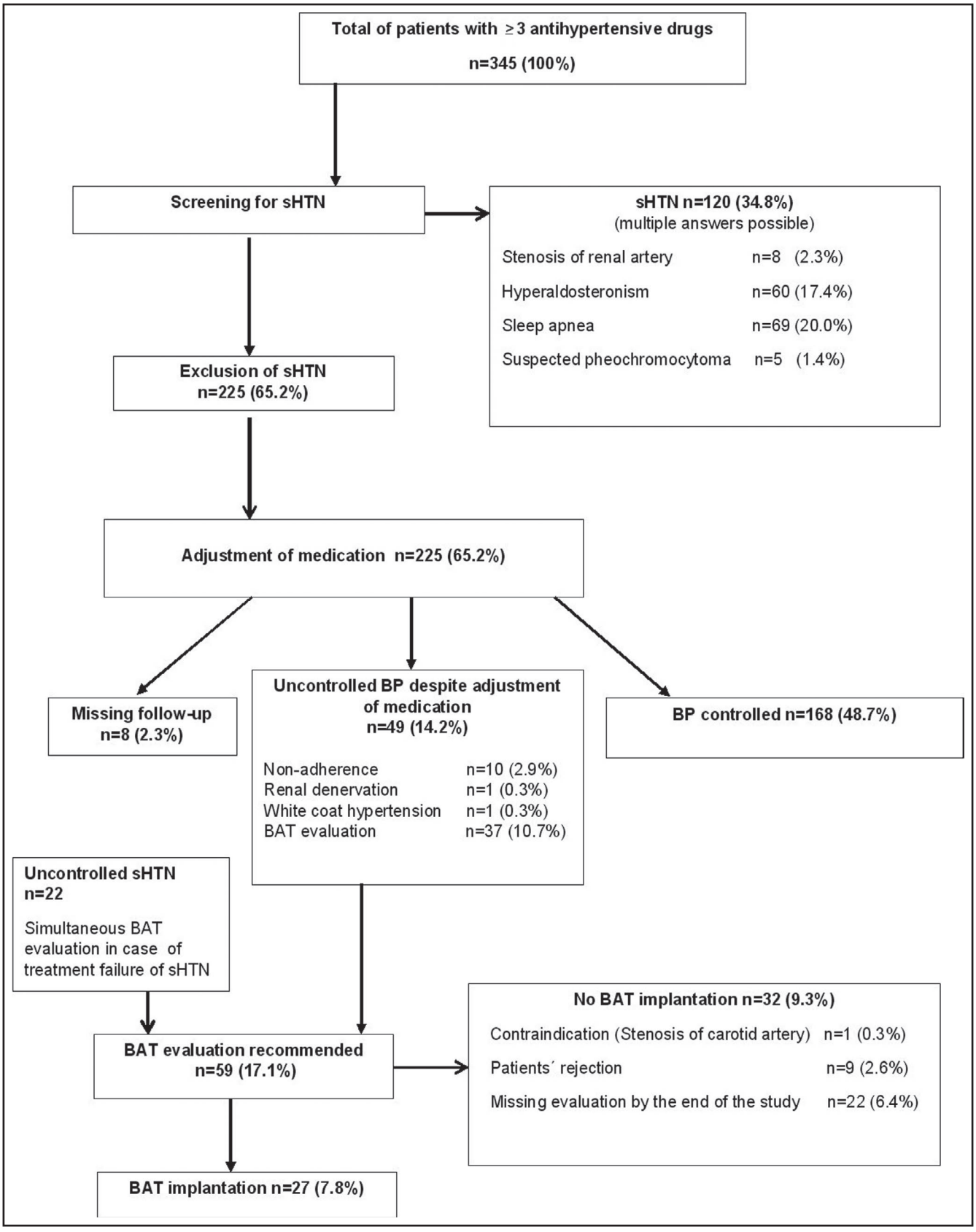

FIGURE 1 Flowchart of BAT indication. BAT—baroreflex activation therapy, BP—blood pressure, sHTN—secondary hypertension

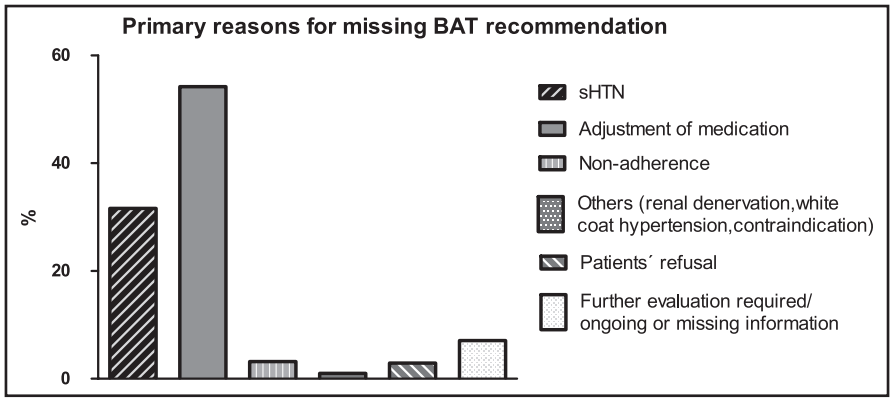

FIGURE 2 Primary reasons for missing BAT recommendation. Several reasons for non-eligibility are possible, and only primary reasons are plotted: main primary reason for non-eligibility was blood pressure adjustment by medication (54.2%), followed by the presence of secondary hypertension (sHTN, 31.6%). Other reasons for non-suitability were required/ongoing evaluation or missing information (7.1%), non-adherence (3.2%), patients' refusal (2.9%) or other reasons like renal denervation, white-coat hypertension, or contraindication (1.0%)

Analyzing patients' need and eligibility for BAT, in our staged assessment, we first screened for secondary causes of hypertension. Thereby we identified a high proportion of patients (34.8%) with secondary reasons for apparently resistant hypertension. Without sleep apnea, sHTN-rate was 21.2% and thus comparable with the results of Florczak et al, who screened 204 patients with resistant hypertension, showing a prevalence of 24% of sHTN, sleep apnea excluded.[31] Taking a closer look at the causes for sHTN, we even saw comparable rates of hyperaldosteronism (17.4% vs. 15.7%) and renal artery stenosis (2.3% vs. 5.4%), whereas we detected much less sleep apnea than this and other studies, possibly due to the use of a different questionnaire.[31,32]

In our study, BAT was recommended to 22 patients with uncontrolled sHTN, most often as a simultaneous evaluation in case of treatment failure of the cause of sHTN. Ultimately, 8 patients with uncontrolled sHTN received a BAT system: 1 patient with hyperaldosteronism refractory to treatment with spironolactone and 7 patients suffering from sleep apnea and persistent hypertension.

In the group of the remaining patients without sHTN, sufficient hypertension control could be achieved by drug adjustment in 74.7%.

Consequently, adjustment of antihypertensive drug treatment was the most common reason for a withdrawn recommendation for BAT. This is in line with the observations of Persu et al, who undertook a comparable study analyzing patients' eligibility for renal denervation.[33] In this study, the most common reason for non-eligibility regarding interventional therapy was successful treatment adjustment, followed by anatomical reasons and sHTN.[33] Another important reason for non-suitability in both our and Persu et al study was poor drug adherence.[33]

In an investigation by Patel et al, non-adherence was even the main cause for non-eligibility for interventional therapy.[11] In this study, comparable to ours, patients' refusal to receive a device-based therapy was also a relevant reason for not proceeding with interventional treatment.

Finally, in our analysis, 17.1% of all evaluated patients received a recommendation for and 7.8% eventually received a BAT system, demonstrating that a precise and standardized evaluation of patients' eligibility for this treatment option should be mandatory. Further studies are needed to evaluate the extent of eligibility in larger patient cohorts.

Analyzing the characteristics of patients to whom BAT was ultimately recommended, these patients were more often male, had a higher BMI, a higher systolic office and ambulatory BP and took a greater amount of antihypertensive drugs than patients without a BAT recommendation. Apart from the BMI, equal characteristics were seen in patients classified as suitable for renal denervation.[33] These findings of particular patients' characteristics could be helpful in future for identifying individuals who are suitable for interventional therapy options.

Concomitant diseases including CKD, HLP, DM, PAD, and stroke clearly occurred more often in patients with a recommendation for BAT, indicating these patients to be at high risk for cardiovascular morbidity and mortality.

Non-adherence is undoubtedly a reason for lack of sufficient BP control and is strongly associated with increasing risk of cardiovascular disease.[10,34,35] Prevalence, however, shows a broad range from 3.3. to 86.1%, depending on the study and applied measure method with clear superiority of objective methods than self-reported measurements.[9]

Using GC-MS, we investigated patients' medication adherence using an objective method which, however, displays some limitations yet.

Some frequently used drugs were not detectable, and our method only allowed a dichotomous yes/no-statement, but none about dosage or regularity of intake. Hence, the majority of drugs was detectable. Unfortunately, a toxicological analysis was not performed in all patients, and for BAT eligibility only patients with reasonable suspicion for incompliance were investigated regarding their medication adherence. For a standardized procedure and in accordance with international guidelines,[8,18] adherence testing should be performed in all evaluated patients prior to BAT implantation.

TABLE 3 Baseline characteristics of patients with and without recommendation for BAT

	Patients with no recommendation for BAT(n = 286)	Patients with recommendation for BAT (n = 59)	p-value
Gender male/female (n)	138/148	40/19	0.0063*
Age (years)	62.1 ± 13.9	62.9 ± 10.6	0.1707
BMI (kg/m²)	30.0 ± 5.7	31.8 ± 5.8	0.0436*
Office SBP (mmHg)	147.7 ± 24.1	168.7 ± 24.7	<0.0001*
Office DBP (mmHg)	84.3 ± 16.1	87.4 ± 18.6	0.3687
24h systolic ABP (mmHg)	144.4 ± 16.8	155.0 ± 14.6	0.0031*
24h diastolic ABP (mmHg)	81.7 ± 12.9	80.8 ± 11.9	0.7714
Amount of antihypertensive drugs	4.4 ± 1.4	5.8 ± 1.3	<0.0001*
CKD	116 (43.8)	35 (59.3)	0.0083*
HLP	136 (53.0)	47 (79.7)	<0.0001*
DM	78 (32.5)	34 (57.6)	<0.0001*
HF	35 (12.5)	8 (13.6)	0.7809
CHD	49 (18.8)	16 (27.1)	0.0747
PAD	8 (4.6)	8 (13.6)	0.0004*
Stroke	13 (5.8)	7 (11.9)	0.0289*
History of smoking	42 (15.1)	10 (16.9)	0.6594

Note: Results are expressed as mean±SD and number (%) respectively.

Abbreviations: ABP, ambulatory blood pressure; BMI, body mass index; CHD, coronary heart disease; CKD, chronic kidney disease; DBP, diastolic blood pressure; DM, diabetes mellitus; HF, heart failure; HLP, hyperlipoproteinemia; PAD, peripheral arterial disease; SBP, systolic blood pressure.

TABLE 4 Adherence to BP medication

	All patients	Patients with sHTN	Medicinally adjusted patients	Patients with no recommendation for BAT	Patients with recommendation for BAT	Patients getting a BAT implantation
Number of adherence tests (n)	75	34	14	47	28	19
Mean amount of detectable drugs (n)	3.89	3.82	3.36	3.70	4.21	3.95
Mean amount of detected drugs (n)	2.92	2.71	3.00	2.47	3.68	3.42
Mean Adherence (%)	75.1	70.9	89.3	66.8	87.4	86.6
Complete Adherence[a] (n (%))	41 (54.7)	17 (50.0)	12(85.7)	26 (55.3)	15 (53.6)	9 (47.4)
Partial Adherence[b] (n (%))	18 (24.0)	8 (23.5)	1 (7.1)	6 (12.8)	12 (42.9)	9 (47.4)
Partial Non-Adherence[c] (n (%))	9 (12.0)	6 (17.6)	0 (0)	8 (17.0)	1 (3.6)	1 (5.3)
Complete Non-Adherence[d] (n (%))	7(9.3)	3 (8.8)	1 (7.1)	7 (14.9)	0 (0)	0 (0)

[a]100% of medication detectable.

[b] ≥ 66 but <100% of medication detectable.

[c] < 66 but >0% of medication detectable.

[d]no medication detectable.

Hence, in our toxicological adherence analysis, only 75 individuals were investigated, mostly independent from eligibility analysis for BAT. One patient classified as non-adherent in the group of individuals with a recommendation for BAT received an adherence analysis *after* BAT implantation.

In our investigation, 78.7% of the patients adhered to at least two-thirds or more of the prescribed drug regimes, and 54.7% even showed complete adherence. Conversely, almost half of patients showed incomplete drug intake and approximately one-fourth of patients was non-adherent, proving non-adherence

to be a relevant issue in the treatment of apparently resistant hypertension.

As expected, the best mean adherence was exhibited by patients with adjusted BP, underlining the meaning of therapy adherence for reaching BP control.

5 | CONCLUSION

In conclusion, mainly due to the identification of treatable reasons for apparently resistant hypertension, only a small amount of evaluated patients (27 (7.8%)) ultimately received a BAT system. Thus, this study—to our knowledge the first report of a staged assessment of patients' suitability for BAT—emphasizes that a precise evaluation of patients' eligibility is highly necessary. It underlines the relevance of a careful examination for this specific interventional antihypertensive therapy option.

Successful adjustment of pharmacologic antihypertensive treatment or the detection of a secondary etiology for hypertension was the most common reason for lack of recommendation for BAT implantation.

Patients with a recommendation for BAT frequently suffer from numerous comorbidities, indicating that these patients are at high risk for cardiovascular morbidity and could potentially greatly benefit from optimized BP control.

Non-adherence was proven to be a relevant issue concerning apparently resistant hypertension and therefore to be an important cause for non-eligibility for interventional therapy.

CONFLICTS OF INTEREST

MW and MK have received speaking honoraria and research grant from CVRx. MK is member of the CVRx Barostim Hypertension Registry Steering Committee. AKS, TK, RWK, DM, EB, ML and MP have no conflicts of interest.

AUTHOR CONTRIBUTIONS

MK and MW designed and supervised the study and undertook the clinical investigation. AKS, TK, DM, and EB performed data collection, and AKS involved in statistical analysis. AKS, TK, RWK, DM, EB, ML, MP, MW, and MK contributed to the interpretation of data. AKS and TK conducted data visualization. AKS prepared original manuscript draft. AKS, TK, RWK, DM, EB, ML, MP, MW, and MK reviewed and edited the manuscript. All authors read, agreed to, and approved the final version of the submitted manuscript.

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