

Differences in patient and physician perspectives on pharmaceutical therapy and renal denervation for the management of hypertension

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Objective: To study patient and physician attitudes to pharmaceutical therapy and renal denervation for the management of hypertension.

Methods: Data were analyzed from 19 market research studies in Western Europe and the United States conducted between 2010 and 2019 to obtain quantitative and qualitative perspectives. The analysis incorporated insights from 2768 patients and the experiences of 1902 physicians either actively performing or interested to perform device procedures, or hypertension specialists who would refer patients for a device-based intervention.

Results: Referring cardiologists and proceduralists were more likely to recommend the renal denervation procedure to patients with higher BP levels and a greater number of antihypertensive medications. Physicians perceived patient reluctance towards a procedure as an important obstacle to recommending renal denervation as a treatment option for uncontrolled hypertension. Patient interest in the renal denervation procedure did not correlate with BP severity ($P=NS$), and the highest preference for the procedure was in patients diagnosed with hypertension but not receiving treatment ($P<0.001$). Patients who perceived high BP as a major problem ($P=0.029$) and those who experienced side effects attributed to their BP medications ($P=0.006$) had a higher preference for renal denervation.

Conclusion: Patients with hypertension often regard the choice of renal denervation to lower BP differently from physicians. A considerable proportion of hypertensive patients, especially those not taking medications, may prefer a device-based approach to reduce their BP.

Keywords: cardiovascular risk, hypertension, patient preferences, renal denervation, shared decision-making, side effects

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; BP, blood pressure; CVD, cardiovascular disease; EU, European Union; SD, standard deviation; US, United States

implementation of both nonpharmacological and pharmacological antihypertensive strategies [1]. Despite the availability of these approaches, the prevalence of blood pressure (BP) control according to societal guidelines remains less than 50% in both economically advanced as well as in developing countries [2–4].

Successful treatment of hypertension in contemporary practice faces several barriers: poor adherence to treatment regimens, physician inertia and insufficient use of combination therapies, among others. In particular, nonadherence is a complex phenomenon involving pill burden, patient reluctance to depend on life-long medical therapy, experiencing adverse events or drug side effects and biased perception of the benefit/risk ratio for drugs [5,6].

In recent years, there has been considerable interest in the potential to reduce BP through device-based approaches, such as renal denervation [7]. This may be an attractive and effective option for patients with hypertension who cannot achieve control with other treatment methods, have elevated cardiovascular risk, and/or whose adherence is challenged by medication intolerance or other factors [8–10].

The importance of a patient–provider shared decision-making process in healthcare is becoming widely recognized [11,12]. Patient preference examines how patients evaluate treatment decisions and how treatment attributes may influence that decision-making process. Specifically, the basis for patient opinions toward treatment options may be very different to that of their physicians. A greater

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INTRODUCTION

Hypertension remains the major preventable cause of cardiovascular disease (CVD) and all-cause death globally, and substantial evidence supports the reduction of adverse clinical outcomes through

understanding of this topic by physicians and healthcare innovators alike is key for the provision of improved care.

Catheter-based approaches including renal denervation represent a new strategy for management of hypertension, yet both patient and provider perceptions specific to renal denervation are largely unstudied. To this purpose, we surveyed patients and physicians in both Western Europe and the United States. The intent was to explore and compare patient and physician attitudes toward hypertension treatments, with particular focus on how they situate catheter-based renal denervation versus pharmacotherapies.

METHODS

Objectives

The purpose of this study was to identify and compare attitudes among both physicians and patients with hypertension toward treatment options of renal denervation and pharmacotherapies. Data were retrospectively analyzed from 19 surveys in Western Europe and the United States conducted between 2010 and 2019. The analysis incorporated insights from 2768 patients and the experiences of 1902 physicians and hospital administrators.

Quantitative and qualitative patient perspectives were collected through in-depth interviews in person and by telephone, examination-room conversations and online surveys, as well as from interviews with treating physicians using a standardized questionnaire with space for open comments. The evaluation was only based on the standardized questions. Market research studies were conducted in accordance with the Council of American Survey Research Organizations Code of Ethics to ensure research integrity and respondent privacy. Surveys were administered blindly, without naming any company or brand and data were checked to ensure validity of responses. All respondents were blinded to the study sponsor. The studies were assessed and included in the analysis if they met standardized quality criteria (e.g. were the research questions clear and suited to the type of inquiry; were sampling, data collection and analysis clearly described; were the claims made supported by sufficient evidence and did the study make a useful contribution?) [13].

Some of the individual studies have published peer-reviewed results [14,15]. Other reports were collected and archived for internal market assessments (Medtronic, Santa Rosa, California, USA) and were made available to the researchers without restriction.

Participants

Surveys of patient perceptions included individuals diagnosed with hypertension, either treated or untreated with antihypertensive medications. The geographical representation included western Europe (France, Germany, Italy, Spain and the United Kingdom) and the United States. Information on physician perspectives was collected in the same countries as patients. Interviewed physicians could be actively performing or interested in performing device-based procedures for hypertension, or hypertension specialists who might consider referral of patients for a device-based intervention. Participants in the surveys gave their informed consent to participate, and ethical approval

was obtained by the appropriate bodies in each region. No responder identity was disclosed at any point.

Study endpoints

Depending on the specific study, patient data included: demographics, time since diagnosis, BP level, duration of antihypertensive medication, self-reported degree of adherence, number of current medications, concomitant medical conditions, experience of side effects, knowledge of hypertension and associated risks, willingness to consider renal denervation and reasons for accepting or rejecting this option. Likelihoods of physician referral or patient acceptance to renal denervation were estimated on a Likert scale from 1 (least) to 5 (most likely), as well as preference, in which a respondent would choose between renal denervation or a pill. Physician respondents were asked about their willingness to prescribe renal denervation for patients depending on the current BP levels and number of BP medications taken. Physicians' impressions of how patients think about device-based or pharmacological therapies were also gathered.

Statistical methods

Data were analyzed descriptively. Categorical variables are shown as frequencies and percentages. Mean and standard deviation (SD) was used to represent continuous variables. Whenever appropriate, the *Z* score test for two population proportions was used to compare categorical variables; continuous variables were compared using unpaired *t* tests. A two-sided *P*-value less than 0.05 was deemed statistically significant. Analyses were performed using IBM SPSS Statistics, version 21 (IBM Corporation, Armonk, New York, USA).

RESULTS

Physician research

Data were available from a total of 1902 physicians and hospital administrators across nine different studies. Most of the data (67%) were collected in 2016–2019. Referring cardiologists and proceduralists were more likely to recommend a patient for renal denervation with higher BP levels and greater number of current medications (Fig. 1).

Interventionalists and referring cardiologists in Europe perceived patient reluctance towards a procedure as an important obstacle to recommending renal denervation for uncontrolled hypertension (Table 1). Other physician-reported needs were support in the guidelines and the peer community, as well as more compelling data. The responses were similar across geographies in Europe and the United States. There were also no relevant differences between the results from earlier and later studies.

Physicians indicated that the primary concern for patients is the invasiveness of the procedure (Table 2). A remaining need to take pills, and uncertainty about long-term effects were further perceived concerns.

Patient research

Data were available from a total of 10 studies which gathered information from 2009 patients. Interviewed patients mostly had high BP despite taking multiple anti-hypertension pills. Close to half the population had a

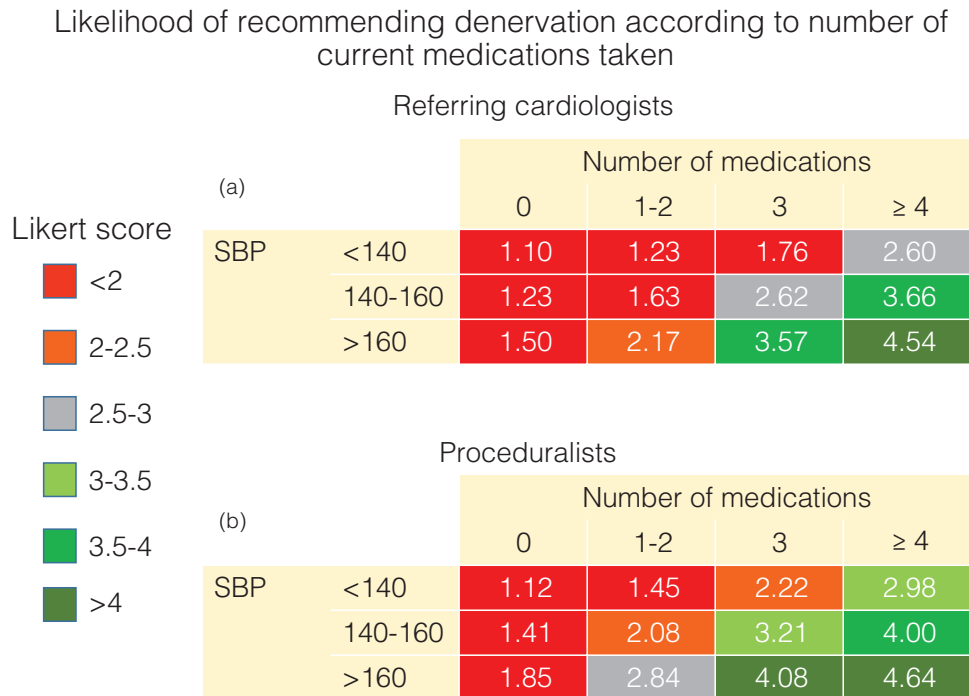


FIGURE 1 Average Likert scores for responses to the question 'On a scale of 1–5, how likely would you be to recommend/refer for/perform on patients with the following characteristics for renal denervation?' according to patients' SBP and number of current medications taken. (a) score for referring cardiologists recommending renal denervation ($n = 286$); (b) score for proceduralists ($n = 246$).

greater than 10-year history of hypertension with 15% reporting more than 20 years since diagnosis (Table 3). Over half (57.9%) the population reported cardiovascular comorbidities. Self-reported adherence rates were high: 81% of respondents considered themselves always to be adherent with their medication regimens, regardless of the experience of side effects and challenging treatment schedules.

In contrast to physician research, patient research ($n = 1666$) found no link between current BP level and willingness to consider treatment with renal denervation (Fig. 2a). Differences between patients with SBP less than 130 mmHg and those with SBP at least 130 mmHg or at least 150 mmHg were not significant ($P > 0.7$ for both). Similarly, there was no obvious relationship between patients' current number of medications and their attitudes towards the renal denervation procedure (Fig. 2b). The greatest willingness to opt for renal denervation over pharmacotherapy was found among diagnosed patients who were yet

untreated, 57% of whom would consider a one-time intervention for their high BP ($P < 0.001$ for difference to patients on antihypertensive medications).

Certain patient characteristics were more frequently associated with a greater willingness to consider renal denervation (Fig. 3). Patients who perceived high BP as a significant problem had a statistically higher preference for renal denervation than those who did not ($P = 0.029$). Patients who experienced side effects attributed to their BP medications also had a statistically higher preference for renal denervation than those who had not experienced side effects ($P = 0.006$).

A comparison of the views of patients with and without comorbidities found a significantly greater proportion of patients with comorbidities willing to consider renal denervation over drugs ($P = 0.049$).

TABLE 1. Major physician-reported hurdles to greater uptake of renal denervation in Europe

Item indicated by physician	Interventional cardiologist ($n = 347$)	Referral cardiologist ($n = 257$)
Patient refuses procedure	38%	42%
Inadequate support in guidelines	30%	30%
Stronger supporting data needed	28%	29%
Needs more support from peer community	26%	32%
Cost concerns	33%	25%

Answers to the question 'Which would you consider the main barriers to recommending renal denervation along with a drug regimen? Select all that apply'.

TABLE 2. Perceived patient concerns about renal denervation as reported by physicians in Europe and the United States

Perceived patient concern reported by physician	Percentage of responders, Europe ($n = 604$)	Percentage of responders, United States ($n = 201$)
Invasiveness of procedure	65%	64%
Will still need to take pills	43%	30%
Unknown long-term effects	47%	61%
Concern about insufficient efficacy	42%	47%
Novelty of procedure	37%	52%
Irreversibility of procedure	29%	24%

Answers to the question 'What are some of the concerns your patients might have about renal denervation? Select all that apply'.

TABLE 3. Characteristics of patients interviewed: n = 2009

Characteristic	n (%)
Age	
<50 years	270 (13.4%)
50–70 years	1107 (55.1%)
>70 years	632 (31.5%)
Male sex	1093 (54.4%)
Hypertension (mmHg)	
<130	304 (15.1%)
130–150	942 (46.9%)
>150	763 (38.0%)
Time since diagnosis of hypertension	
<10 years	1151 (57.3%)
10–20 years	557 (27.7%)
>20 years	301 (15.0%)
Number of medications taken for hypertension	
0	72 (3.6%)
1	685 (34.1%)
2	433 (21.6%)
3	535 (26.6%)
≥4	284 (14.1%)
Self-reported adherence (n = 1937)	
Never–sometimes	59 (3.0%)
Usually	315 (16.3%)
Always	1563 (80.7%)
Comorbidities present (n = 591)	342 (57.9%)

Physicians were the main sources of information about medical conditions and treatments for patients with hypertension, both in Europe and in the United States. A physician's recommendation was the single most important positive factor influencing patients' readiness to undergo

renal denervation. The promise of reduced BP with the intervention was an additional driver of acceptance and approximately one-third of those asked would be influenced by the experiences of other patients. However, in research from the United States, 45% of patients indicated a refusal to undergo renal denervation even if the procedure were recommended by their physician.

DISCUSSION

The overall finding of the current analysis of a large number of market research studies in the European Union and United States is that patients with hypertension may regard the choice of an intervention to lower BP differently from physicians, and a sizable proportion of patients prefer renal denervation to reduce their BP. With the emergence of catheter-based interventions, such as renal denervation as an alternative approach to pharmacotherapies for hypertension [16–19], the differences in attitudes are highly relevant and may have implications for both how treatment recommendations are made by healthcare providers, received by patients and taken into account by payers.

Whereas physicians appeared to base treatment considerations on measurable factors, that is, BP and number of medications currently taken, no such relationship between higher BP and/or more medications and a preference for renal denervation was found in patient research. Patients most likely to prefer the renal denervation procedure had greater understanding of the risks associated with hypertension from either personal experience or health literacy, and thus had strong motivation to control their BP. Although other variables, not included in our study, may

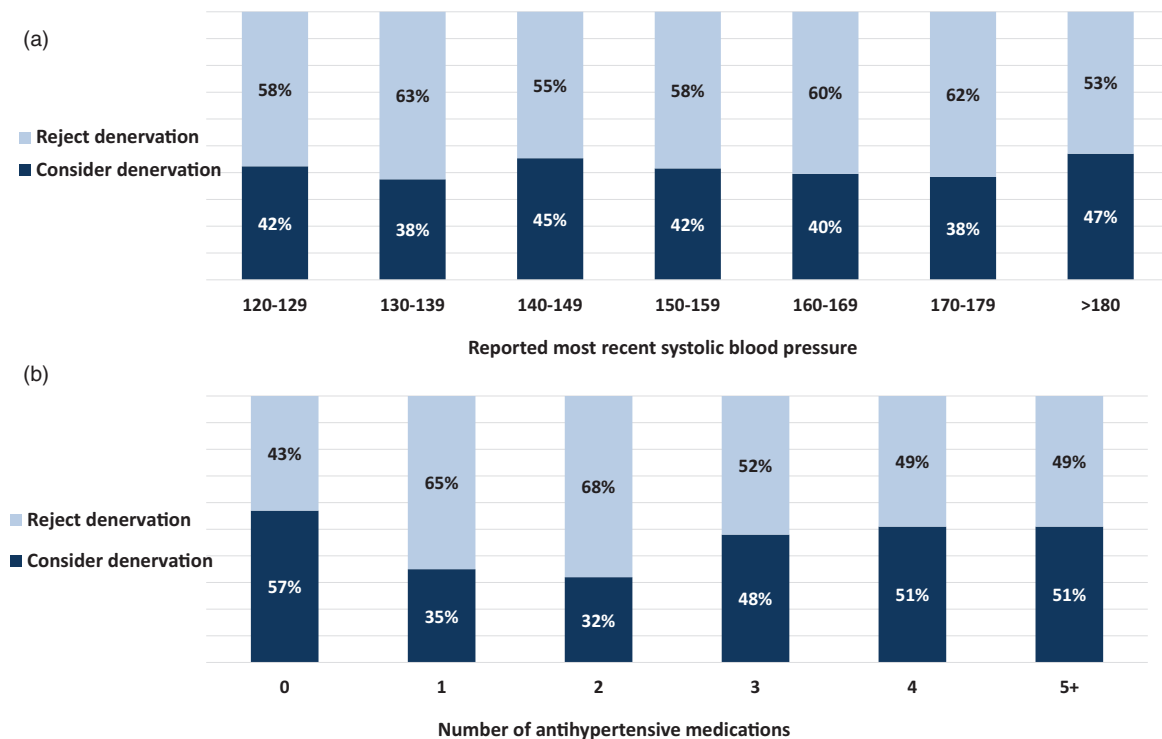


FIGURE 2 Percentage of patients who would consider renal denervation according to most recently measured SBP (a; n = 1666) and to the number of antihypertensive medications currently taken (b; n = 1717).

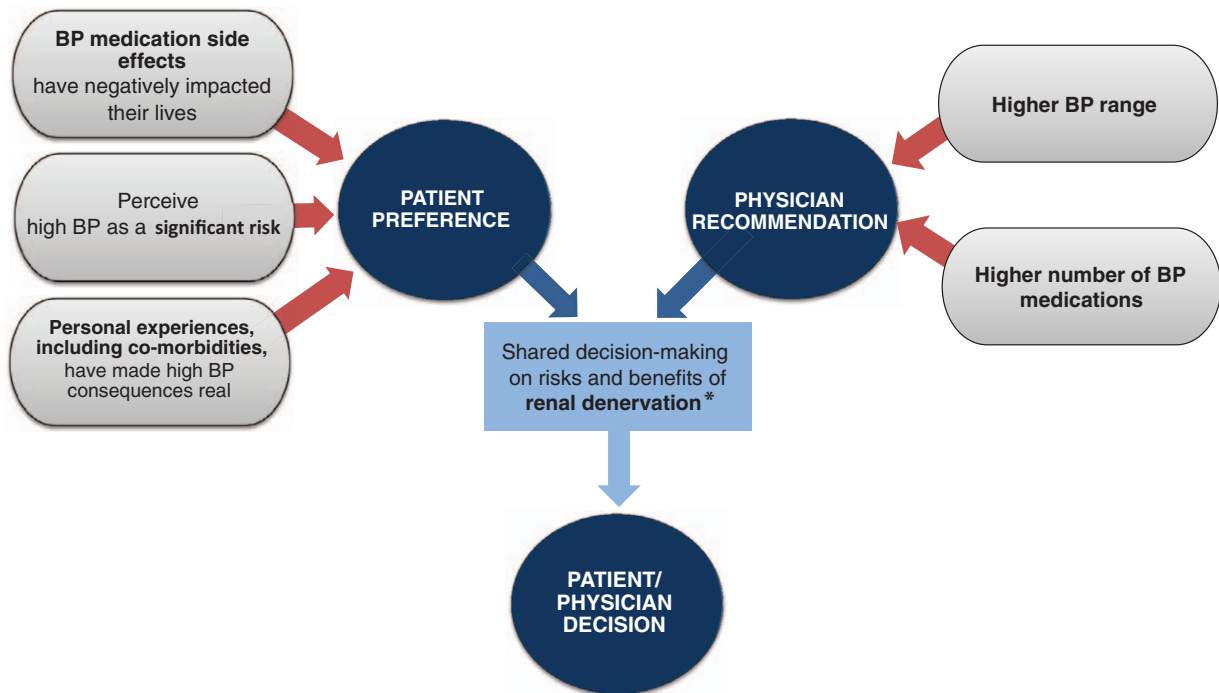


FIGURE 3 Factors influencing patient and physician perspectives on renal denervation. Patient preference for renal denervation is shaped by the perception of high blood pressure (BP) as a risk, having personally experienced the consequences of high BP (including comorbidities), or having suffered from medication side effects. BP levels and medication burden determine a physician's recommendation for renal denervation. *A physician's recommendation was the single most important positive factor influencing patients' readiness to undergo renal denervation.

also influence preferences, this disparity between physician and patient perspectives has not been previously described in this setting.

The rationale for physician preference for a catheter-based intervention is uncontroversial within the clinical community and indeed reflects what is currently recommended in treatment guidelines for hypertension in regard to stages of hypertension [1]. As a confirmation that physicians are by and large practicing evidence-based medicine, this is a reassuring finding. To resolve the tension between patient and physician attitudes to treatment, a dialogue between caregiver and patient is needed about the risks and benefits of various treatment approaches and patient preference.

Radiofrequency renal denervation is the first catheter-based procedure for hypertension to be made available (in the European Union; still investigational in the United States). Hence, it is not surprising that patients' main concerns focus on the interventional nature of the procedure. With a new pharmaceutical agent, obvious points of comparison with current medications are efficacy, convenience, side effects, experienced and unknown (e.g. skin cancer with thiazide-like diuretics and lung cancer with ACEIs, recent pollution of valsartan), patient perception about 'Big Pharma' and feelings about taking drugs in general. An invasive procedure comes with different potential benefits and concerns and is difficult to compare directly with drugs. Patients take into account benefit and risk when considering hypertension and treatment, but their priorities, as well as understanding and acceptance of risks and side effects, can vary widely [20,21]. The irreversibility of an ablation procedure is in contrast to pills, which can be discontinued

in case of an unacceptable efficacy/tolerability relation. However, our data suggest that only a minority of patients may see this as an issue with an interventional procedure. The need to continue with pills even after a device-based procedure appears to be a concern for some patients, but not others, which may reflect the frequent comorbidities and associated pills beyond BP-lowering treatments in individuals with hypertension.

A spectrum of patient preferences and attitudes to illness and therapy has been described for other invasive treatments, such as catheter ablation for atrial fibrillation or device approaches for obesity [22,23]. Patients are increasingly recognized as partners in healthcare decisions, with different experiences and viewpoints of disease and treatment. Enabling patient choice in healthcare is known to increase individual knowledge of treatment modalities and improve the decision quality, matching it closer to patient values [24].

For patients, we identified physician recommendations to be the single most compelling factor for patients who were likely to consider catheter-based renal denervation. Patients who perceived high BP as a significant problem had a statistically higher preference for renal denervation than those who did not. Personal experiences of consequences of hypertension as well as side effects from treatments also influenced attitudes. Such personal experience is likely to drive a search for additional education and alternative therapies. Higher levels of health literacy have been associated with greater adherence to treatments for chronic as well as acute conditions [25]. But educational tools must incorporate and engage patient perspectives and experiences [5]. This is particularly relevant with newly

emerging treatments, placing the responsibility for this awareness on healthcare providers when engaging with patients.

Although more confirmatory studies would be needed, it appears that patients, regardless of their current level of BP and pill count, are equally open to renal denervation. This stands in stark contrast with the perspective of many physicians, which suggest that only those patients with very high BP on three or more medications would be appropriate candidates for renal denervation, based on available clinical evidence at the time the surveys were conducted. This may be relevant to the future of interventional hypertension medicine as well as for discussions with reimbursement bodies. Given its favorable safety profile [16,17,19], a discussion is currently ongoing in Europe about the most suitable target population for renal denervation [26]. The different views between healthcare stakeholders uncovered in the current analysis illustrate the need to involve patients more closely in discussions and to incorporate shared decision-making into the care pathway. Understanding patients' perspectives will enable a more efficient use of clinical practice resources and improve the options for access to the most suitable treatment for individual patients [27].

The main strength of the analysis is the large number of surveys and respondents, who came from various countries and were recruited in several ways, from cardiology offices and study enrolment campaigns to online surveys. The wide range of characteristics increases the external validity of these findings to the general population of people with hypertension. Study data were also obtained from physicians' discussions with patients, which provided a different perspective from what patients may express in direct interviews or questionnaires. A limitation is the lack of a standardized instrument to survey patients' preferences for hypertension management. Patients' concerns in the United States, where renal denervation is not yet available, were overall somewhat stronger than in Europe, where the procedure has been an option for a few years and real-life experiences are available. A direct comparison of patients' views between these regions is thus probably not valuable. A further limitation is that while various efforts were made to optimize the clarity of questions (e.g. pretests to evaluate the use of terminology), there was no standardized assessment of patients' educational level and socioeconomic status. There is a possibility of bias; for example, physicians may be unwilling to express views that diverge from guidelines. This is likely to have been minimal, however, as results were consistent across various surveys and conducting entities (commercial market research organisation or academic institution). Moreover, the included surveys spanned the time before and after the publication of the positive renal denervation trials in 2017–2019 [16,19], but not the recently published SPYRAL HTN-OFF MED Pivotal trial [28] and the question of a possible shift in perceptions with the new findings has not been addressed.

In conclusion, patients frequently held views of hypertension treatments and renal denervation, which diverged from those of treating physicians. Specifically, patients most likely to accept renal denervation were those with the

perception of high blood pressure as a risk, having personally experienced the consequences of high BP (including comorbidities), or having suffered from medication side effects. Physicians were most likely to recommend renal denervation for the most severe patients, on multiple meds and high BP, even though those patients may not be more likely to accept an intervention. Further studies, preferably using a standardized instrument to survey patient preferences for hypertension management, would be important to ensure individualized access to the most suitable treatment options.

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Conflicts of interest

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