National Institute for Health and Care Excellence

IP1938 Alcohol-mediated perivascular renal denervation for resistant hypertension

IPAC date: 14 November 2024

Com. no.	Consultee name and organisation	Sec. no.	Comments [sic]	Response Please respond to all comments
1.	Consultee 1 British and Irish Hypertension Society (BIHS)	General	The BIHS supports the NICE recommendation that more research is needed. Studies to determine whether the procedure is best employed in certain patient groups and the long term efficacy, are needed.	Thank you for your comment.
2.	Consultee 2 British Cardiovascular Society (BCS)	General	No comments but I agree with the recommendations.	Thank you for your comment.
3.	Consultee 3 NHS Professional	General	I am an NHS consultant involved in the investigation and management of hypertension. I have been a local investigator, and recruited subjects, for trials of renal denervation using all of the currently available technologies (radiofrequency, ultrasound and now alcohol-mediated) renal denervation. The interventional procedures guidance on percutaneous transluminal renal sympathetic denervation for resistant hypertension (www.nice.org.uk/guidance/ipg754; March 2023) was limited to the radiofrequency and ultrasound methods based on the published data available at the time. That guidance recommended that the procedure should only be used with special arrangements for clinical governance, consent, and audit or research. The current interventional procedures consultation document addresses alcohol-mediated perivascular renal sympathetic denervation for resistant	Thank you for your comment. The committee has considered your comment but decided not to change the 'research only' recommendation. The committee makes recommendations based on its assessment of the evidence on the efficacy and safety of that individual interventional procedure, but the committee does not compare the procedure with other similar

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			hypertension. In contrast to the previous document, the current consultation document concludes that more research is needed on the alcohol-mediated technique and that procedures should only be done as part of a formal research study with research ethics committee approval. I question why this guideline reaches a different conclusion to that for the radiofrequency and ultrasound techniques. The randomised trial of alcohol-mediated renal denervation in resistant hypertension was of a similar size (or larger) to the trials in similar patient groups using the other technologies. There was a modest (but statistically significant) difference in BP reduction between the active and sham treated groups of broadly similar magnitude to that shown in trials of the other technologies. The procedure appears to be safe. While there are limited safety data from the trial of alcohol-mediated renal denervation in resistant hypertension, there are longer term safety data from other trials using the same technology in different patient populations. Hypertension remains a problem in the UK with poor rates of control and a significant population with resistant hypertension. While renal denervation is clearly neither the solution to, nor a cure for, hypertension, the combined evidence suggest that it may have a role to play through modest but clinically meaningful reductions in blood pressure. Unfortunately, despite all the clinical trials and experience to date, it is still not possible to identify those patients who are likely to respond. Further experience, including by careful data collection within registries, may help to clarify this and identify those who may benefit the most, as well as providing further longterm efficacy and safety data. I would argue that there are sufficient efficacy data to support the use of alcohol-mediated renal denervation in the resistant hypertension patient	interventions. The rationale behind the recommendations is detailed in the guidance ('why the committee made these recommendations'). IPG754 is included in the 'related NICE guidance' section of the overview, and was considered by the committee in their deliberations.

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			group and adequate longterm safety data from all trials of the technology. I would therefore support the use of this technology under the same special arrangements (for clinical governance, consent, and audit or research) as those applied to the radiofrequency and ultrasound techniques.	
4.	Consultee 4 Ablative Solutions, Inc.	General	Renal denervation is a novel, targeted, one-time, minimally invasive procedure for patients with persistent hypertension, despite medicinal therapy, as well as in patients with hypertension when not taking antihypertensive medications or not compliant with a prescribed medication regimen. This therapeutic approach has been done safely using energy (radiofrequency and ultrasound) and alcohol-mediated denervation. Alcohol mediated renal denervation has several advantages to escalation of pharmacologic therapies: 1) AH medications are not as effective in more resistant populations, and patient compliance is a known issue. Thus, there is a need for these one-time procedures in the treatment paradigm. 2) Alcohol denervation is a relatively quick procedure causing minimal discomfort to patients, with modest (outpatient) sedation. 3) It does not require substantial training and can be done reproducibly by a skilled interventional cardiologist/radiologist. 4) This approach may have cost-effectiveness related to a single patient-use catheter, medical grade alcohol, with no requirement for capital equipment. NICE published guidance on energy-based devices for renal denervation (IPG754) in 2023; this guidance recommended “should only be used with special arrangements”. We have taken this evidence-based guidance as	Thank you for your comment. The committee has considered your comment but decided not to change the ‘research only’ recommendation. The committee makes recommendations based on its assessment of the evidence on the efficacy and safety of that individual interventional procedure, but the committee does not compare the procedure with other similar interventions. The rationale behind the recommendations is detailed in the guidance (‘why the committee made these recommendations’). IPG754 is included in the ‘related NICE guidance’ section of the overview, and was considered by the committee in their deliberations.

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			our precedent to compile our feedback, as these procedures are similar one-time catheter-based interventions, with the only difference being the mechanism by which the nerves are being ablated (e.g. form of energy vs a neurolytic agent). As noted by the Committee, energy-based RDN is expected to be used in a joint decision-making process for patients who are not controlled by medication and lifestyle changes alone. It is important to compare the body of evidence for alcohol-mediated denervation in that “On Med” population to what has been published for the energy-based devices. It is acknowledged that there were differences in defined primary outcomes (e.g. timepoints, mean vs median, 24-hour vs Daytime BP). To truly compare these trials, we have summarized the primary endpoints by 24-hour reduction from baseline in our written feedback (Sept 25th 2024). It is important to put into context that in the TBPI trial (n=300), more than half the subjects were taking more than three AH medications, a more difficult to treat population compared to the other ON Med trials for energy-based devices. Within our written feedback (Sept 25th 20240, we have also made note of language in specific sections of the draft guidance that we believe should be reconsidered. Specifically, as it relates to the summation of sedation use and summary of safety. We respectfully request the committee to reconsider their recommendation and consider a similar recommendation to that given for the energy-based devices. This will ultimately allow patient care providers (under special controls), to determine what is the best treatment option for the patients under their care.	In terms of comments on specific sections of the draft guidance, please see responses to comments 6 to 8.

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5.	Consultee 5 NHS Professional	General	As we know, HTN remains a global health concern. Even in the UK, 1 in 3 or 4 adults have HTN and control rates remain poor. There is a huge unmet clinical need for novel therapies in HTN to reduce CV risk. The alcohol mediated (chemical) renal denervation procedure is similar to other energy-based procedures, with similar body of evidence in support of the use of these specific procedures. Recommendations for alcohol based RDN should not be more restrictive than what NICE has published on energy-based devices. Alcohol Mediated Neurolysis has a long history as a safe and effective treatment in various conditions requiring nerve block or neurolyses. The body of safety data for local administration of alcohol for these purposes is already well documented in the literature. The use of alcohol for this specific indication in the perivascular area around the renal arteries has been studied in 5 completed trials, with 2 being RCTs, in over 350 treated arteries. We were the second largest site globally on these RCTs and as a result have good experience in using this therapy and device. I would recommend the use of alcohol mediated RDN in HTN patients with resistant and uncontrolled HTN. Also important to note, alcohol mediated denervation may have other important advantages: • Consistent circumferential denervation with single infusion per artery • Not as dependent on user / operator “takes out guess work” • Minimal injury to media (no energy exposure to the vessel walls) • Single-use catheter – without the burden of capital equipment (generator)	Thank you for your comment. The committee has considered your comment but decided not to change the ‘research only’ recommendation. The committee makes recommendations based on its assessment of the evidence on the efficacy and safety of that individual interventional procedure, but the committee does not compare the procedure with other similar interventions. The rationale behind the recommendations is detailed in the guidance (‘why the committee made these recommendations’). IPG754 is included in the ‘related NICE guidance’ section of the overview, and was considered by the committee in their deliberations.

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			• Less painful • Short procedure time – less radiation / contrast	
6.	Consultee 5 NHS Professional	2.4	The committee noted that *"the procedure is usually done under local anaesthesia, with deep sedation and anticoagulation".* This procedure does not require deep sedation as it is relatively painless compared to other therapies. Patients were not able to work it out if they had active or sham treatment.	Thank you for your comment. The wording 'deep' has been removed from section 2.4 of the final guidance.
7.	Consultee 5 NHS Professional	3.3	The committee noted that *"The professional experts and the committee considered the key safety outcomes to be: pain, bleeding, damage to renal arteries or other structures, and transient microleaks of alcohol."* As noted above, pain associated with this procedure is less severe compared to that reported for other recommended energy-based RDN procedures. Also, for clarification, the transient microleaks reported during this procedure are not alcohol leaks. Alcohol is infused into the perivascular space around the renal arteries. The transient microleaks reported in the literature are defined as small amounts of blood that exit the artery after the 32-gauge microneedles are retracted, similar to the drop of blood you have on your arm after a flu vaccination. These were reported as peri-procedural adverse events to capture the incidence of this occurrence, however it is important to note that these microleaks resolve quickly (often within seconds) and have no resultant clinical sequelae. These patients were followed by repeat scanning that did not show any safety concerns on imaging.	Thank you for your comment. Reference to 'transient microleaks of alcohol' has been removed from section 3.3.
8.	Consultee 5 NHS Professional	3.7	The committee noted that *"this is an invasive procedure, so more evidence is needed on safety."* As noted, this minimally invasive procedure has been used safely across five completed studies to date. Adverse events were rare,	Thank you for your comment.

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			and did not result in any untoward long term clinical deficits or required interventions. 6-month imaging has shown preservation of renal artery patency. Kidney function is also preserved.	Extra wording has been added to section 3.7 of the final guidance.

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