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Robot-assisted renal denervation as a new surgical approach for therapy resistant arterial hypertension

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ABSTRACT

Arterial hypertension is a major cause of mortality and morbidity worldwide. Medical therapy is the most common treatment. However, in some cases there is a persistent high blood pressure despite medical therapy. These patients with medication refractory arterial hypertension can be treated by renal denervation. Until now an endovascular approach has been used. There are however limitations in eligibility based on vascular or anatomical anomalies. For these patients, as well as other patients eligible for renal denervation, robot-assisted renal denervation has the potential to become a surgical treatment option based on our findings.

1. Declaration of interest statement

The authors have no conflicts of interest to declare that are relevant to the content of this article.

2. Introduction

Hypertension is the major risk factor for coronary artery disease and stroke potentially leading to premature death. Despite good monitoring of blood pressure, approximately 10 % of patients have resistant, uncontrolled hypertension. Hypertension is usually defined as resistant or refractory when a therapeutic plan, that includes consideration of lifestyle methods and a prescription of at least three different antihypertensive drugs (including a diuretic) in optimal doses, has failed to diminish both systolic and diastolic blood pressure (BP) to threshold of 140/90 mmHg.[1,2] The aim by lowering the blood pressure is a systolic blood pressure of less than 130 mmHg. Using anti-hypertensive drugs, every 10 mmHg reduction in systolic blood pressure significantly reduces the risk of cardiovascular events, coronary heart disease and heart failure which leads to a significant 13 % reduction in all-cause mortality.[3]

In most patients with idiopathic hypertension there is a sympathetic overactivity which is mainly regulated by the renal afferent and efferent nerves. This overactivity stimulates the Renin-Angiotensin-Aldosterone-System (RAAS) with more arterial vasoconstriction and tubular reabsorption of sodium and water resulting in higher tensions. On the other hand, less renal blood supply causes feedback to the hypothalamus which in turn provokes sympathetic stimulation again 4. These important sympathetic peri-arterial renal nerves are extensively anatomically described by Sakakura K., Ladich E., Cheng Q. et al..[5]

Renal denervation (RDN) aims at switching off this sympathetic overactivity. Different percutaneous catheter-based techniques have been used including radiofrequency ablation systems, alcohol injections and balloon-based techniques.[6,7] The SPYRAL ON MED trial showed that patients treated with RDN compared with sham control had a significant 10 mmHg systolic BP reduction after 36 months follow-up independent of concomitant medications and without significant side effects.[7] Current European Society of Hypertension guidelines recommend RDN in patients who have uncontrolled BP despite the use of antihypertensive drug combination therapy or if drug treatment elicits serious side effects [class II, level of evidence B].[2] Compared with the standard treatment of care for blood pressure reduction, RDN is a cost-effective treatment for patients aged <65 years with an initial absolute 10-years predicted cardiovascular risk of at least 13.2 %[8]

However, not all patients with refractory hypertension qualify for percutaneous RDN mainly because of inappropriate renal vascular anatomy such as renal arteries <3mm or >8mm or multiple accessory renal arteries supplying >25 % of the parenchyma. Usually, also patients with advanced stage chronic kidney disease with an eGFR<45 ml/min

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Abbreviation

AHA	Antihypertensive Agents
RDN	Renal Denervation
RA-RDN	Robot-Assisted Renal Denervation

or increased bleeding risk were excluded from the trials because it is described as contraindicated.[1,9,10]

Based on the limitations of the endovascular procedure, the need of a surgical alternative emerged thus the Robot-Assisted Renal Denervation (RA-RDN) was developed. While maintaining the benefits of minimally invasive surgery, the endowrist technology of robotic instruments provides a greater and also more accurate range of motion. This is useful knowing that the most important orthosympathetic nerves are located distally.[5] This treatment option may be an alternative to the endovascular RDN because it can also be used in more complex cases with vascular and anatomical variations.[8–10]

3. Case presentation

3.1. Case

A 43-year old man without further medical history was referred. He had a long-standing history of hypertension starting drug therapy at the age of 18 years old with increasing numbers of medications. In the last five years, his blood pressure continued to rise resulting in more symptoms (agitation, headaches, chest pain, sweating, epistaxis, etc.) and more need of antihypertensive drug therapy, currently refractory to a 9-component maximal drug regimen (Table 1). Nonetheless, the patient had multiple hypertensive crises mandating multiple hospital admissions for intravenous therapy.

Several investigations excluded secondary causes of arterial hypertension. No family history of arterial hypertension was present. All endocrinological tests were repeatedly negative. No renal artery stenosis was seen on magnetic resonance imaging (MRI) arteriography. However, an anatomical variant of the renal arteries was present with 3 arteries on the left and 4 arteries on the right (Fig. 1). All of these arteries were patent and clinically significant since the diameter was more than 3mm making the patient not eligible for percutaneous RDN.

An interventional treatment was needed to stabilize the blood pressure and to avoid new crises. Certainly because of his young age and the risk of developing major health risks (10-year predicted cardiovascular risk score of 16 % life expectancy) due to the increasing blood pressures as well has his daily medical burden. Therefore, after intensive multidisciplinary counselling the decision was made to perform a Robot-Assisted Renal Denervation (RA-RDN).

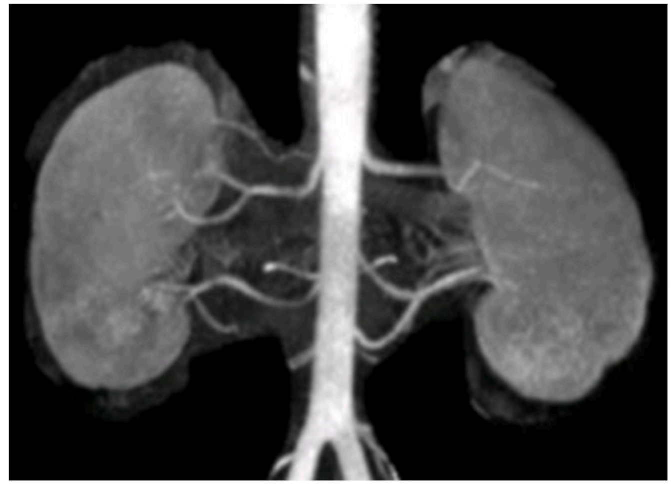

Fig. 1. MRI arteriogaphy showing 3 left renal arteries and 4 right renal arteries.

3.2. Material and methods

The surgical procedure was performed under general anaesthesia with arterial monitoring and an adequate venous access. The surgical team consisted of a surgeon, a bedside assistant and a scrub nurse. The patient was placed in the right lateral flank position for the best anatomical exposure and access to the left renal arteries. One assistant port (12mm) was placed 3cm supra-umbilically. Carbon dioxide was insufflated to generate an intra-abdominal pressure of 12 mmHg. Subsequently the 4 robotic ports (8mm) were placed based on a paramedian line technique, 8cm in between, starting with a robotic port located 2 fingers breadths under the costal margin 10.

Then the Da Vinci Xi robot was docked with focus on the left kidney. Placement from cranially to caudally: bipolar forceps, camera, monopolar scissors and prograsp.

First the retroperitoneum was assessed and the aorta was identified. Then systematically the 3 left renal arteries were identified, dissected and carefully looped. The magnetic resonance images were regularly consulted to safely retrieve all arteries. Subsequently the peri-arterial tissue, including the nerves, were fully stripped, divided and cauterized from their aortic origin to as distal as possible. This was followed by haemostasis and drain placement in the retroperitoneal space.[10] The trocar ports were closed using an intradermal suture and the assistant port was preserved sterile. All the instruments were kept sterile while the patient was repositioned on his left lateral flank. Then a similar procedure was performed with dissection of the 4 right renal arteries.

Table 1
Pre-operative antihypertensive drug therapy.

1. Olmesartan + Amlodipine + Hydrochlorothiazide 40/5/25mg 1×/day
2. Spironolactone 50mg 1×/day
3. Moxonidine 0.6 mg 1×/day
4. Hydralazine 50mg 4×/day
5. Nebivolol 7,5mg 2×/day
6. Alprazolam 0,25mg 3×/day
7. Tamsulosin 0,4mg 1×/day
8. Amlodipine if necessary

Table 2
Antihypertensive drug therapy at the hospital during the post-operative period.

1. Olmesartan + Amlodipine + Hydrochlorothiazide 40/5/25mg 1×/day
2. Spironolactone 25mg 1×/day
3. Moxonidine 0.4 mg 1×/day
4. Hydralazine 75mg 1×/day

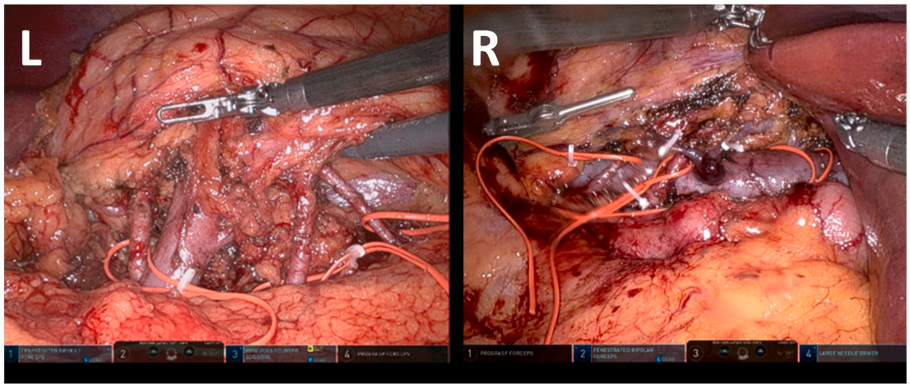

Fig. 2. Complete renal denervation: panel A = left side (L), panel B = right side (R).

The complete renal denervation is showed in Fig. 2.

The operation was completed in 3 hours and 15 minutes with negligible blood loss.

After the procedure the patient was referred to the intensive care unit for post-operative monitoring. After 24 hours he was referred to the urological unit. The 2 abdominal drains were extracted on day one. Intravenous fluid suppletion cessation was obtained on day two due to adequate oral fluid intake. After switching to oral analgesics, the patient could be discharged from the hospital on the third day after surgery. Several visits at the emergency department followed in the weeks after surgery, each time due to pain complaints. Investigations (blood tests, computed tomography) showed reassuring findings allowing discharge with conservative management.

4. Results

Pre-operatively an average 24 hours ambulatory mean blood pressure of 181.0/105.5 mmHg was measured with multidrug treatment (Table 1). Peri-operatively the blood pressure remained stable. The first 24 hours post-operatively at the intensive care unit, a mean blood pressure of 160.42/74.42 mmHg was measured with the use of noradrenaline and without any antihypertensives.

After the immediate post-operative period the patient experienced a remarkable reduction in agitation. From then on, a normotensive blood pressure was obtained with a median of 130.25/77.88 mmHg in combination with a reduced combination of antihypertensives (Table 2).

After discussion with his cardiologist, moxonidine was stopped at the time of discharge. At two weeks, further tapering of his medication was possible with hydralazine dose reduction to 25mg daily. A few days later a complete cessation of hydralazine intake was possible due to a persistent systolic blood pressure <140 mmHg. One month after the procedure episodes of dizziness and fatigue were present. Subsequent blood pressure measurement showed a hypotensive blood pressure. Therefore, at this time all the antihypertensives were stopped after consulting his cardiologist. Six weeks post-operatively, 24 hours ambulatory blood pressure monitoring showed a mean blood pressure of 123.2/77.6 mmHg without any treatment. Five months post-operatively, 24 hours blood pressure monitoring was repeated, showing a mean blood pressure of 137.3/87.5 mmHg. Except for some sensitivity in the supra-umbilical region he did not report any other symptoms. This blood pressure evolution is displayed in Fig. 3.

5. Discussion

We present the unique case of a young patient with therapy refractory idiopathic hypertension, turned down for percutaneous RDN in the presence of 7 unique renal arteries that was successfully treated with RA-RDN.

While the observed 24 hours systolic ambulatory BD reduction at 6-months follow-up in contemporary trials such as SPYRAL ON MED is generally considered to be modest (−1.9 mmHg),[6] it seems that the observed treatment effect in our patient was much more pronounced. In our patient we noted a reduction in blood pressure of 43.7 mmHg systolic and 18.0 mmHg diastolic pressure after a follow-up of five months, while all antihypertensive agents were stopped. Previous studies showed that the density of orthosympathetic nerves increases progressively with increasing distance from the ostium. Additionally, in a percutaneous approach the nerves that are located at the outer border of the vessel may be incompletely targeted. Therefore, it seems plausible that a surgical approach would result in more profound and more complete orthosympathetic denervation.[5]

In an earlier era, non-randomized studies showed that surgical sympathectomy was an effective treatment for some patients with uncontrolled hypertension, but profound orthostasis commonly occurred after the procedure. To the best of our knowledge, this is the first time that a robotic approach was used in a patient with very complex renal

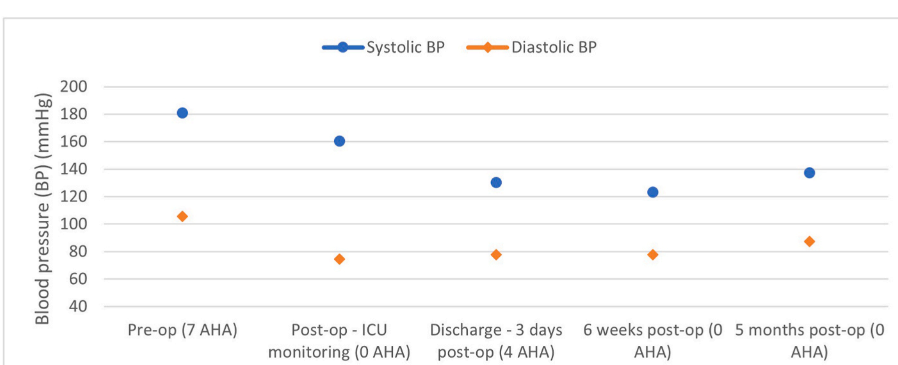

Fig. 3. Evolution of blood pressure (BP) and antihypertensive agents (AHA) in the peri-operative period.

vascular anatomy.

The prevalence of arterial hypertension is increasing worldwide. Despite good medical compliance, some patients develop adverse effects to antihypertensive agents.[1,10] Endovascular renal denervation as a salvage treatment for refractory hypertension is increasingly being used although trials did not show a significant reduction in blood pressure so far.[1] Considering the contra-indications for this intervention (e.g. patients with chronic kidney disease, anatomical variations), some patients need an alternative in complex cases of hypertension.[10] Surgical renal denervation may be proposed as an alternative in selected patients. Our first experience with this approach has shown a spectacular reduction in blood pressure with cessation of all antihypertensive agents.

Of course, our results are based on the findings in one patient which can only serve as a proof-of concept, while the RDN trials were adequately powered randomised trials. Further investigation of the surgical approach is needed to increase our understanding of this technique and to check which patients might benefit from this approach. Based on previous experiences, we should also be cautious to induce profound hypotension which is usually very difficult to manage pharmacologically.

This technique has the potential for wide adaptation as it can be safely performed by any robotic or laparoscopic surgeon who is confident performing renal surgery, e.g. partial nephrectomies. The robotic assisted approach does help in dissecting all arteries completely in a safe manner.[10]

6. Conclusions

Arterial hypertension is a major cause of mortality and morbidity worldwide. Medical therapy is the most common treatment. However, in some cases there is a persistent high blood pressure despite medical therapy. In these cases, secondary causes should be excluded, e.g. endocrinological conditions. If no other causes can be found, these patients with medication refractory arterial hypertension can be treated by renal denervation. Until now an endovascular approach has been used. There are however limitations in eligibility based on vascular or anatomical anomalies. For these patients, as well as other patients eligible for renal denervation, robot-assisted renal denervation has the potential to become a surgical treatment option based on our findings. In contrast to the endovascular approach, we believe no vascular or anatomical exclusion criteria are present. It appears to be a feasible surgical technique for surgeons performing renal surgery. Long term follow-up and data of more patients are however needed to evaluate the value and success rate of this treatment option complementary to the endovascular approach.

CRediT authorship contribution statement

Sarah Rosier: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Visualization, Writing – original draft, Writing – review & editing. **Robby Lamoury:** Writing – original draft, Writing – review & editing. **Koen Ameloot:** Conceptualization, Data curation, Investigation, Methodology, Writing – review & editing. **Robbe Knaepen:** Writing – review & editing. **Thomas De Sutter:** Writing – review & editing. **Hans Goethuys:** Writing – review & editing. **Yannic Raskin:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Writing – original draft, Writing – review & editing.

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All authors contributed equally to the study conception and design. Data collection and analysis were performed by Rosier Sarah, Lamoury Robby, Ameloot Koen and Raskin Yannic. The first draft of the manuscript was written by Rosier Sarah and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

The authors affirm that the participant provided an informed consent, also for publication of the images in Figs. 1–2.

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