Endovascular Treatment of Nutcracker Syndrome

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Background: Nutcracker syndrome, or mesoaortic compression of the left renal vein (LRV), with associated symptoms related to venous hypertension in the left kidney, is a rare entity that may result in severe symptoms requiring operative intervention. We report on 3 patients who presented with nutcracker syndrome, including one patient with a circumaortic LRV resulting in posterior nutcracker syndrome, who underwent successful endovascular treatment with renal vein stenting. A review of existing literature on endovascular management of nutcracker syndrome follows.

Methods: Three women (age range 28–43 years) presented with symptoms and imaging studies consistent with nutcracker syndrome. Symptoms included pelvic and flank pain in all 3 patients, and episodes of hematuria in 2 patients. Imaging studies demonstrated compression of the LRV between the superior mesenteric artery and aorta in 2 of the patients. The third patient was noted to have a circumaortic LRV.

Results: All 3 patients underwent venography and LRV stenting. Stents included a 12 × 40 mm self-expanding nitinol stent, 14 × 60 mm WALLSTENT, and 16 × 40 mm WALLSTENT. All patients were placed on clopidogrel postoperatively. The duration of follow-up ranged from 6 to 27 months. At follow-up, all 3 patients reported significant symptomatic improvement, and duplex ultrasonography demonstrated stent patency in all.

Conclusions: Nutcracker syndrome is a rare condition that can be successfully treated with renal vein stenting via an endovascular approach. Results are encouraging at follow-up periods beyond 2 years.

The nutcracker phenomenon, or entrapment of the left renal vein (LRV) between the aorta and superior mesenteric artery (SMA), was first described by Grant in 1937. The SMA normally originates from the aorta at a right angle and proceeds in a ventral direction before turning caudal. This prevents entrapment of the LRV, coursing between the anterior SMA and the posterior aorta. When the SMA arises from the aorta at a more acute angle or the LRV takes an abnormally high course, compression of the LRV can occur. The name nutcracker syndrome (NCS) was coined to describe the constellation of symptoms that occur as a result of venous hypertension in the left kidney caused by mesoaortic compression of the LRV. The symptoms reported most commonly are left flank or pelvic pain and hematuria. Additionally, pelvic congestion and varicocele formation can occur in women and men respectively, as a result of reflux into the left gonadal vein, which serves as a major collateral pathway for drainage of the left kidney. When symptoms are severe, operative intervention may be necessary.

Both open and endovascular approaches to the treatment of this condition have been described in the literature. Open surgical options include LVR or left gonadal vein transposition, renal auto-transplantation, and LRV bypass. Endovascular LRV stenting was first described in 1996 by Neste.
et al.8 Since that time, outcome data have been limited to a handful of series and case reports.3,5,6,9 Herein, we report on 3 patients who presented with imaging studies and physiological findings consistent with NCS, including one patient with a circumaortic LRV. All patients underwent successful endovascular LRV stenting with resultant improvement in symptoms.

CASE REPORT

Case 1: A 29-year-old previously healthy female presented with intermittent pelvic and flank pain and episodes of gross hematuria of 1 year duration. During this interval, she was hospitalized several times and underwent an extensive diagnostic work-up, which included consultation with a gynecologist, urologist, and nephrologist. Routine laboratory studies, including coagulation factor assays, were all within normal limits, while urinalysis showed macroscopic hematuria, without evidence of urinary tract infection. Urine cytology was negative for malignancy. Evaluation with computed tomography (CT) demonstrated compression of the LRV between the aorta and SMA, an enlarged left ovarian vein, and multiple large pelvic collateral vessels (Fig. 1).

Conservative management was attempted; however, the patient was significantly disturbed by her symptoms and elected to proceed with treatment. Both open and endovascular treatment options were considered. The risks and benefits of each approach, including the lack of long-term follow-up data on renal vein stenting, were extensively discussed with the patient. Although the patient’s symptoms were significant enough for her to desire an intervention, this young female patient did not wish to proceed with open surgery because she did not wish to have an abdominal incision. The decision to proceed with an endovascular approach was ultimately made by the patient, after a balanced discussion about the risks and benefits of both open and endovascular intervention.

The patient was taken to the operating room and venography was performed via left common femoral vein access. Pelvic venography demonstrated marked reflux in the left ovarian vein, which was approximately a centimeter in diameter. Additionally, there was severe stenosis of the mid portion of the LRV from extrinsic compression by the SMA. Renocaval pullback pressure was 8 mm Hg. The area of stenosis was treated with balloon angioplasty using 5, 10, and 16-mm balloons.

Fig. 1. Venography (A) and CT (B) demonstrating compression of the LRV between the aorta and SMA, as well as an enlarged left ovarian vein, consistent with findings of NCS. Following stent placement in the LRV, venography (C) and CT (D) demonstrate improved venous outflow from the kidney.
A 16- × 40-mm WALLSTENT was then placed across the area of stenosis, with part of the stent extending into the renal pelvis and part of the stent protruding into the inferior vena cava (IVC). An excellent technical result was achieved. Postoperatively, the patient was placed on 75 mg clopidogrel daily, for a duration of 1 year. The hematuria resolved; however, she continued to complain of pelvic pain. Two years following the initial operation, she underwent repeat venography. This demonstrated findings consistent with pelvic congestion syndrome (PCS), including a large left gonadal vein and significant collateral vessels communicating with both hypogastric veins. Embolization of the gonadal vein was performed using 1% sodium tetradecyl sulfate (STS) solution mixed 1:1 with heparinized saline as well as intravenous contrast. Coil embolization was then performed with one 9-mm coil and one 7-mm coil. Completion venography demonstrated cessation of flow in the left gonadal vein. At follow-up, 27 months following the initial operation, she was doing well, with significant symptomatic improvement and duplex studies demonstrating patency and good position of the LRV stent.

Case 2: A 28-year-old woman with a history of median arcuate ligament syndrome treated with open ligament release and subsequent celiac axis stent placement for residual stenosis presented with persistent abdominal pain of several years duration. She had undergone an extensive diagnostic work-up to elucidate the source of her abdominal pain, including upper endoscopy and diagnostic laparoscopy, which failed to show any pathology. Imaging studies, including CT angiography, demonstrated the celiac stent to be widely patent; however, there was evidence of LRV compression between the aorta and SMA and she was referred to us for treatment of NCS. Given the patient’s young age and lack of long-term follow-up data on renal vein stenting, we initially attempted to treat the LRV stenosis with balloon angioplasty. Selective venography demonstrated moderate-to-severe stenosis at the proximal renal vein. The gonadal vein was large and provided the dominant outflow to the kidney. An attempt was made to use intravascular ultrasound (IVUS) to obtain pressure measurements in the LRV; however, the ultrasound probe would not advance past the stenosis and therefore this was aborted. An 8-mm balloon was then used to perform angioplasty of the venous stenosis. Following this, there was much-improved venous outflow through the main renal vein.

The patient’s symptoms improved for only a week following the intervention. Additionally, she reported symptomatic improvement when resting in the right lateral decubitus position. An attempt was made to use intravascular ultrasound (IVUS) to obtain pressure measurements in the LRV; however, the ultrasound probe would not advance past the stenosis and therefore this was aborted. An 8-mm balloon was then used to perform angioplasty of the venous stenosis. Following this, there was much-improved venous outflow through the main renal vein.

Case 3: A 43-year-old female presented with abdominal and pelvic pain, dyspareunia, and microscopic hematuria. An appropriate work-up, which included urinalysis and urine cytology and hematologic and gynecologic evaluation, failed to reveal any abnormalities. She was evaluated with magnetic resonance imaging (MRI) and CT and found to have massive pelvic varicosities, as well as a circumaortic LRV (Fig. 3). Venography was performed to further delineate the patient’s venous anatomy. A cavo-gram, performed via a right common femoral vein approach, demonstrated a circumaortic LRV, with the lower portion being retroaortic. The LRV was catheterized both superiorly and inferiorly. The lower portion was
stenotic based on compression between the aorta and the spine. The upper portion had severe fibrotic stenosis. IVUS confirmed a 1-cm area of severe stenosis at the junction between the LRV and the IVC. Pelvic venography demonstrated a large ovarian vein with severe reflux into the pelvis and massive pelvic collaterals around the bladder. Balloon angioplasty of the superior portion of the LRV was performed using a 5-mm balloon and then a 7-mm balloon. Finally, a 14 × 60 WALLSTENT was placed across this lesion. Postdeployment balloon angioplasty of the WALLSTENT was performed using a 10-mm and subsequently 12-mm balloon. Completion venography demonstrated an excellent technical result (Fig. 4). Although she reported some improvement following this, the patient remained significantly symptomatic with regards to her PCS, suggesting persisting reflux of her left ovarian vein into her pelvic varicosities despite relief from the central obstruction at the renal vein. Hence, 3 months later, she underwent successful embolization of the left ovarian vein with 1% STS solution (described in Case 1) and coils, including two 9-mm coils and one 7-mm coil. Following this, the renal vein was reimaged. Both the left anterior and posterior renal venous components of the circumaortic renal vein were widely patent. The patient continued clopidogrel daily for a 1-year duration. Seven months following the initial operation, the patient reported significant improvement in her symptoms.

**DISCUSSION**

NCS is a rare entity that may result in severe symptoms requiring operative intervention. The condition occurs most frequently in women in the third and fourth decades of life and typically manifests itself as flank and pelvic pain and hematuria.\(^2\) NCS should be regarded as a diagnosis of exclusion and initial patient assessment should focus on a complete work-up to exclude alternate causes of pain and hematuria. A thorough history should be elucidated and complete physical examination should be performed. Laboratory studies are an important adjunct in excluding other etiologies of pain and hematuria. In particular, urine culture and cytology should be assessed to exclude a malignant or infectious process as a cause of patient symptoms. Cystoscopy, flexible ureteroscopy, or renal biopsy may be indicated depending on laboratory results.

Following a thorough history, physical examination, and laboratory studies, assessment of patients should include noninvasive imaging studies before venography is undertaken, because diagnostic imaging may similarly aid in distinguishing NCS from other causes of pain and hematuria. Options include MRI, CT, and ultrasonography.\(^3\) On ultrasonography, renal outflow must be assessed to look for obstructive lesions. The presence of collateral pathways should be determined, and in particular the presence or absence of reflux in the left gonadal vein should be evaluated. LRV stenosis is considered significant if the anteroposterior diameter of the LRV on the left side of the aorta is 5 times greater than that at the level of the stenosis and if the peak velocity at the stenosis is 5 times the peak velocity at the hilum.\(^15\) The sensitivity and specificity

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**Fig. 3.** MRI demonstrating a circumaortic LRV. Compression of the anterior and superior LRV segment between the aorta and SMA results in anterior NCS (A). Compression of the posterior and inferior segment of the LRV between the aorta and spine results in posterior NCS (B).
of duplex scanning in diagnosing NCS is 78% and 100% when flow reversal in the collateral veins is included in the diagnostic criteria. CT and MRI serve to further define the anatomy of the LRV in relation to surrounding structures, to identify cases of a retroaortic or circumaortic LRV, and to exclude other sources of pain and hematuria, including malignancy of the urinary system and nephrolithiasis.

Posterior NCS refers to compression of a retroaortic LRV between the anterior aorta and posterior spine. It is estimated that in 0.5–3% of the population the LRV takes a retroaortic course and in 0.3–5.7% the LRV is doubled in a preaortic and retroaortic course as a circumaortic LRV, thus making posterior NCS a much more uncommon finding than anterior NCS. Our patient #3 had circumaortic renal veins and thus had a component of posterior NCS. We chose to address the anterior renal vein in this patient, as this was the more hemodynamically significant lesion. Reports of intervention for posterior NCS are rare and limited to open repairs.

Once a diagnosis of NCS is suspected based on noninvasive imaging studies, and the severity of symptoms warrants potential intervention, selective LRV venography should be performed. This may be done through a femoral, internal jugular, or brachial vein approach. On venography, the diagnosis of NCS will be supported by compression of the LRV with contrast stasis, varicose veins, and collateral pathways. If possible, the renocaval pullback pressure gradient should be measured. A gradient of $<1 \text{ mm Hg}$ is normal and a gradient of $\geq 3 \text{ mm Hg}$ is considered indicative of renal hypertension.

When symptoms are severe and imaging studies support a diagnosis of NCS, operative intervention may be considered. Children should be treated conservatively because spontaneous remission can occur during growth. It has been observed that 75% of patients younger than 18 years old will have complete resolution of hematuria within 2 years of presentation. Similarly, asymptomatic patients with incidental findings of mesoaortic LRV compression should be managed conservatively, as the natural history of such findings is not well delineated.

Once the decision to intervene is made, both open and endovascular surgical options may be considered. Open intervention was first reported by Pastershank in 1974. Options include LVR transposition into the IVC 3–5 cm below the previous origin, renal autotransplantation, and LRV bypass, among others. Open repair for NCS represents the standard of care to date and has proven to have excellent outcomes with mid- to long-term follow-up. For example, Reed et al. reported that during a mean follow-up of 39 months, symptoms of flank pain and hematuria improved in 80% and 100% of their 11 patients treated with LRV transposition. Two preoperatively occluded LRVs rethrombosed; one underwent thrombolysis with stenting, the other reimplantation of the left gonadal vein into the IVC. In agreement with these outcomes, Hartung et al. reviewed open surgical intervention for NCS and reported resolution of symptoms in 35 and improvement in 5 of the 42 patients. In patients treated with LRV transposition, 17 of 18 became asymptomatic with recurrent hematuria in 1 patient. Open operative management offers good results, but is inherently invasive and carries

![Fig. 4. Pre- (A) and poststenting (B) venograms of the circumaortic LRV.](image)
the risk of significant bleeding and injury to the left ureter and other surrounding structures.

Endovascular LRV stenting for the treatment of NCS was first described by Neste et al. in 1996.9 Results from several large studies are encouraging.3,5,6 Wang et al.7 performed a retrospective review of 30 patients treated with endovascular stent placement between 2004 and 2010. All patients received one 14 × 60-mm self-expanding nitinol stent (SMART stent, Cordis). Three patients with severe left-sided varicoceles underwent gonadal vein embolization. The median duration of follow-up was 36 months. Technical success was achieved in all patients and no perioperative complications were reported. At 1-month follow-up, all patients achieved symptomatic improvement, including 2 patients who had persistent but decreased hematuria. All stents were patent on duplex scan and there was no secondary recurrence of the symptoms at the end of the follow-up period. Two cases of stent migration were diagnosed at 12 months. Both stents protruded into the IVC; they were left in situ with uneventful follow-up at 49 months and 56 months. The authors concluded that endovascular treatment is a safe, effective, and minimally invasive technique that provides good long-term patency rates for patients with NCS. The study participants, however, were all Asian, 93% were men, and the mean age of the group was 18 years (range 13–32); therefore the results of this study may not translate to the slightly older, predominantly female patient population that is typically treated for NCS in the Western hemisphere.

In a larger, retrospective review of 61 patients who underwent LRV stenting between 1998 and 2009, Chen et al.8 similarly assessed the long-term efficacy and safety of endovascular stenting for NCS. The median age of this study population was 26 years and 75% of patients were male. The median duration of follow-up was 66 months. Stents of variable sizes were used and included 1 Palmaz stent, 15 WALLSTENTS® and 45 SmartControl™ stents that were 10, 12, 14, or 16 × 40 mm. The authors reported that symptoms (hematuria, proteinuria, and flank pain) resolved or improved in 15 patients at 1 week, another 24 patients at 1 month, and another 20 patients at 6 months. Symptoms were unchanged in 2 patients and recurred in 1. One perioperative complication occurred with the stent being deployed in an LRV collateral, requiring open operative intervention. Three postoperative complications occurred including stent migration into the right atrium, stent protrusion into the IVC, and stent migration into LRV hilum. The authors recommend endovascular stenting as primary treatment for NCS.

To date, the largest Western hemisphere study on endovascular treatment of NCS comes from a French group who reported on 5 patients who underwent successful LRV stenting between 2002 and 2004.9 All patients received WALLSTENTS, which measured between 16 and 20 mm in diameter and 40–60 mm in length. One case of stent migration into the retrohepatic vena cava was reported with a 20- × 60-mm stent. Attempts were made to reposition the stent with the use of an endovascular snare; however, this was unsuccessful and the stent was left in the IVC just cephalad to the LRV. A second stent, measuring 16-mm in diameter, was successfully deployed in the LRV of this patient. At 1 month follow-up, patients all reported symptomatic improvement, and all stents were patent on duplex scan examination. Pelvic pain recurred in 1 patient who had initially improved following treatment, and endometriosis was diagnosed 15 months after the procedure. Two other patients, who received 40-mm-long stents, had a secondary recurrence of the symptoms caused by stent dislodgement. These patients were managed with close surveillance. The remaining 2 patients were asymptomatic at follow-up. The authors advocated for the use of longer stents that protrude into the IVC to minimize the risk of stent migration.

Additional cases of stent migration have been reported in the literature,20–22 and this remains one of the feared complications of endovascular treatment of NCS. To minimize the risk of migration and improve outcomes, the ideal stent should have high radial strength, and be conformable with little shrinkage in length to allow for accurate placement. We recommend use of intravascular ultrasonography to obtain precise LRV diameter measurements in order to facilitate stent size selection. There is no consensus in the literature regarding the extent to which renal vein stents should be oversized. Wang et al.7 placed stents of a single size (14 × 60 mm) in all their study patients, resulting in significant variability in the degree of oversizing (3–40%). In our practice, we oversize by approximately 20%. More importantly, we attempt to engage the stent at the level of the first-order branch of the renal vein to minimize the risk of stent migration. Finally, we advocate for use of balloon-expandable stents over self-expanding stents, when possible, to ensure precise stent placement. We do not recommend venoplasty before stent placement in all patients, as NCS results from mechanical compression of the renal vein and is not the result of a primary luminal stenosis. Selective venoplasty may be performed to facilitate stent placement, for instance in cases where the stenosis is difficult to traverse.
There are no standard guidelines on the use of anticoagulants or antiplatelet medications to improve stent patency following LRV stenting. Our patients were placed on 75 mg clopidogrel daily and all stents remained patent on follow-up imaging studies. Although LRV stent thrombosis is seldom reported in the literature, possibly due to the local release of urokinase,23 use of antiplatelet agents or anticoagulants remains a concern in the management of NCS. Therefore, our patients were placed on 75 mg clopidogrel daily and all stents remained patent on follow-up imaging studies.

Finally, additional intervention for the treatment of PCS or varicocele formation may be required in conjunction with treatment of NCS. Two of our 3 patients required embolization of the left ovarian vein due to continued pelvic pain. Both of these patients improved significantly following the second procedure. Embolization of the gonadal vessels should not be performed before LRV stenting, as early embolization of the gonadal vein may exacerbate NCS by eliminating an important outflow vessel for the left kidney. Based on our experience, however, we now recommend ablation of the gonadal vein at the time of LRV stenting in patients with clear evidence of pelvic congestion to avoid the need for reintervention.

The management of NCS continues to evolve. This rare condition should be regarded as a diagnosis of exclusion and other etiologies to account for patient symptoms should be investigated before attempts at treatment. Treatment should be limited to patients with severe symptoms who have failed conservative management. When the endovascular approach to treatment is chosen, we advocate for the use of IVUS for precise vessel measurement, stent oversizing by 20%, use of balloon-expandable stents when possible, engagement of the stent at the level of the first-order branch of the renal vein, and ablation of the gonadal vein during the initial intervention in patients with PCS. Open repair for NCS remains the standard of care with excellent long-term outcomes. However, endovascular LRV stent placement appears to offer similarly good results in the short term. Long-term outcomes, in a characteristically young patient population, remain to be determined. Improvement in the technology for venous stents is expected and will likely result in endovascular treatment of most cases of NCS in the future.

REFERENCES