AJR WOMEN'S IMAGING

Time-Resolved MR Angiography as a Useful Sequence for Assessment of Ovarian Vein Reflux

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OBJECTIVE. The purpose of this retrospective study was to assess the imaging characteristics of ovarian vein reflux using time-resolved MR angiography (TR-MRA). One hundred consecutive female patients underwent TR-MRA of the pelvis to evaluate suspected or known pelvic pathology. Findings of ovarian vein reflux, ovarian vein dilation, and periuterine varices were analyzed and correlated with symptoms of pelvic pain.

CONCLUSION. Overall, TR-MRA is a useful sequence for the assessment of ovarian vein reflux, which may aid the evaluation of pelvic congestion syndrome.

Pelvic congestion syndrome (PCS) is defined as chronic pelvic pain caused by incompetent ovarian veins, with associated venous reflux and venous engorgement [1–4]. It is estimated that approximately 10% of women have incompetent ovarian vein valves and that of these, approximately 40% experience chronic pelvic pain directly as a result of venous congestion [5].

Several noninvasive techniques are used for workup of potential PCS cases, including ultrasound, CT, and MRI [1, 6–9]. Static CT and MRI rely on the detection of ovarian vein dilation and early filling of the ovarian veins, although neither can accurately determine whether flow is anterograde or retrograde. The direction of flow is of particular importance because the generally accepted cause of PCS is retrograde venous flow in an incompetent ovarian vein [1–4]. Accordingly, treatment via ovarian vein ligation or embolization to prevent ovarian vein reflux has shown high success rates and is the current first-line therapy [3, 4, 10]. Furthermore, pelvic veins tend to dilate under certain situations, such as prolonged standing or coitus. Therefore, while the patient is supine for CT or MRI, abnormal ovarian veins with incompetent valves may be nondilated and therefore may not be detected on static CT or MRI.

Conventional angiography is currently considered the gold standard for the detection of PCS [2]. However, this procedure is time-consuming, invasive, and necessitates the use of ionizing radiation. Furthermore, the injection of contrast material into the origin of the ovarian veins alters the normal physiologic hemodynamics within the veins, potentially making conventional angiography less specific.

Time-resolved MR angiography (TR-MRA) has been proven to be a quick and noninvasive technique that allows visualization of the physiologic blood flow dynamics. This technique has been shown to be highly sensitive for detecting pathology in a variety of blood vessels and body parts when compared with conventional angiography [11–14]. TR-MRA is predicted to be helpful for the detection of PCS because of its presumed ability to accurately determine whether anterograde or retrograde flow in the ovarian vein is present. The purpose of this study was to evaluate the utility of TR-MRA for detecting ovarian vein reflux and to describe its associated imaging characteristics.

Materials and Methods

This retrospective study was approved by the institutional review board, and a waiver of informed consent was obtained. The radiologic database was reviewed for all female pelvic MRI studies performed at our institution using a TR-MRA protocol during a 5-month period. A total of 100 consecutive women (median age, 43 years; age range, 16–86 years) were included in this study. Sixty of the patients were parous with an average parity of 2.1. The most common indications included uterine leiomyoma (n = 46), adnexal mass (n = 30), and pelvic mass (n = 11). Other less common indications included menorrhagia (n = 4), suspected uterine anomaly (n = 2), chronic pelvic pain

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($n = 2$), suspected ovarian vein thrombosis ($n = 1$), suspected salpingo-oophoritis ($n = 1$), and genital symptoms ($n = 1$). No patients carried a diagnosis of PCS.

Each study was independently reviewed by two board-certified radiologists with 10 and 8 years of experience with vascular MRI. The radiologists were blinded to all demographic and clinical information. Anonymized images were reviewed on a freestanding workstation (Advantage Windows, GE Healthcare). The presence and laterality of retrograde ovarian vein flow and the presence of ovarian vein dilation were determined for each patient. In case of differing interpretations, a consensus read was performed. These cases were further analyzed for the presence of ovarian vein dilation greater than 7 mm, periuterine varices, and time elapsed until ovarian vein opacification [7]. Additionally, findings compatible with nutcracker syndrome as an anatomic cause of PCS were also assessed, including the angle of the superior mesenteric artery (SMA) to the aorta (normal > 60°), left renal vein diameter on the basis of coronal maximum-intensity-projection images, and continuity of flow from the left renal vein into the inferior vena cava (IVC) [15]. The medical records for all patients were reviewed for symptoms of chronic pelvic pain.

Time-Resolved MR Angiography Protocol

Imaging was performed with a magnetic field strength of 1.5 T ($n = 63$ [Magnetom Avanto, Siemens Healthcare]; $n = 25$ [Signa HDx, GE Healthcare]) or 3 T ($n = 12$ [Magnetom Tim Trio, Siemens Healthcare]). The imaging protocols are summarized in Table 1. Signal reception was performed using dedicated body array coils. Two time-resolved techniques were used, either the Time-Resolved Angiography With Interleaved Stochastic Technique (TWIST, Siemens Healthcare) (75 patients) or the Time-Resolved Imaging of Contrast Kinetics (TRICKS, GE Healthcare) (25 patients). Patients were placed in the supine position with their arms at their sides. During shallow breathing, imaging of the pelvis was performed in the coronal plane at rapid 2- to 5-second intervals for 1–3 minutes after peripheral IV injection of 0.1 mmol/kg body weight of nondiluted gadopentetate dimeglumine (Magnevist, Bayer HealthCare) or gadobenate dimeglumine (MultiHance, Bracco Diagnostics) at a rate of 2 mL/s. This was followed by a saline bolus of 20 mL at 2 mL/s. Maximum intensity projections of each 3D data set were generated in both the coronal and sagittal planes. Data were displayed as cine loops consisting of up to 60 coronal or 60 sagittal images.

Statistical analysis was performed using Graphpad Software (Graphpad). Left renal vein diameters were compared between patients with and without ovarian vein reflux and between parous and nonparous patients using the unpaired Student's t test. Correlation between parity and left ovarian vein reflux was analyzed using the Fisher's exact test.

Results

Of 100 women who underwent MRI of the pelvis with the TR-MRA sequence, a total of 10 (10%) were diagnosed with retrograde flow within the left ovarian vein (Table 2 and Figs. 1 and 2). No cases of right ovarian vein reflux were identified. The average time of appearance of retrograde ovarian vein opacification after initial aortic enhancement was 15 seconds (range, 7–32 seconds). Of the 10 patients with ovarian vein reflux, eight were parous (80%) with an average parity of 1.8. Of the 90 patients without ovarian vein reflux, 52 (58%) were parous, with an average parity of 1.3 (p = not significant).

Periuterine varices were identified in eight patients, six of whom had ovarian vein reflux. A dilated ovarian vein was identified in 11 patients, seven of whom also had ovarian vein reflux (Fig. 3). Therefore, of the 11 patients with ovarian vein dilation or periuterine varices (which would likely be visualized on static CT or MRI), the time-resolved component allowed differentiation of the seven patients who had actual ovarian vein reflux from patients with normal anterograde ovarian venous flow.

Three potentially false-positive cases were identified involving venous flow in a caudal direction originating from the left renal hilum (through nonovarian veins): a retroaortic renal vein with inferior insertion to the IVC in two patients and collateral vein insertion to the left common iliac vein in one patient.

Further inspection of the TR-MRA images revealed that three of the patients with left ovarian vein reflux had probable nutcracker syndrome as the underlying cause of the left ovarian vein reflux (Fig. 2). In these three patients, the angle between the SMA and IVC was abnormally acute (35°, 36°, and 44°; normal, > 60°) [15]) with apparent discontinuous flow between the left renal vein and IVC. Furthermore, the left renal vein diameters for these three patients (16.3, 15.5, and 12.6 mm) were markedly larger than the average left renal vein diameter (± SD) of the patients without ovarian vein reflux (10.1 ± 1.8 mm). The average left renal vein diameter in patients with left ovarian vein reflux (13.0 ± 2.7 mm) was significantly larger compared with patients without reflux ($p < 0.0001$).

Review of the medical charts revealed that 40 patients had symptoms of pelvic pain, although 36 had coexisting pathology that can cause pelvic pain (Table 2). Five of 10 patients with ovarian vein reflux had symptoms of chronic pelvic pain that could potentially be attributable to PCS (Table 2). However, three of these five patients had additional findings that can also cause pelvic pain. One of these patients had adenomyosis and a single submucosal fibroid, and one had multiple fibroids. One patient had undergone transarterial uterine fibroid embolization but with persistent pelvic pain.

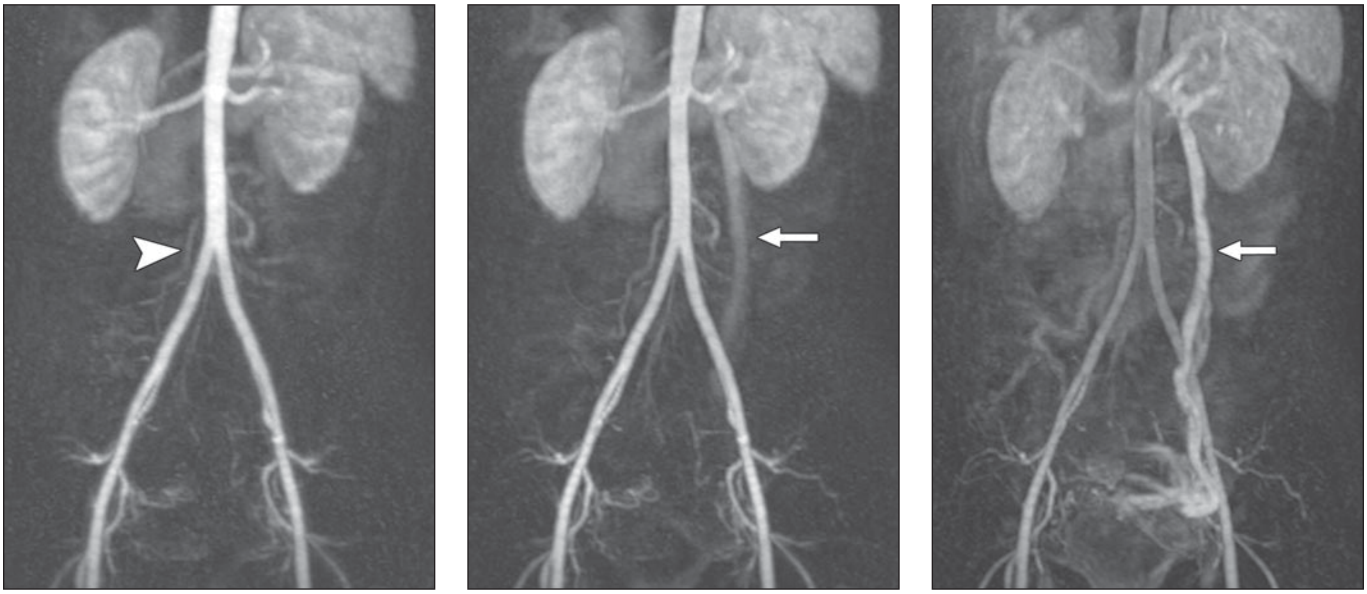
Discussion

The prevalence of retrograde flow in the ovarian veins has been estimated at 9.9% based on 273 angiographic studies on healthy female renal transplant donors, with 59% of them reporting chronic pelvic pain compatible with PCS and 77% reporting improvement after ovarian vein ligation [5]. Our study population showed a similar prevalence in a selected population. It should be noted that the incidence of ovarian vein reflux in our study is not expected to be representative of the general population because only women with pelvic symptoms or pathology underwent MRI. Although there are numerous studies that have directly or indirectly correlated ovarian vein reflux with PCS, the actual significance of ovarian vein reflux is still debatable, considering that our and other studies have shown ovarian vein reflux in asymptomatic women [6–8].

A number of studies have reported radiologic findings of retrograde flow in the ovarian veins on the basis of CT and static MRI [4, 6–9]. All of these studies diagnosed ovarian vein incompetence on the basis of ovarian vein dilation and the presence of early opacification in the arterial phase. However, with static images, it can be very difficult or impossible to definitively ascertain whether flow is anterograde or retrograde, particularly if image acquisition occurred in the later aspect of the arterial phase. As our study showed, ovarian veins can be dilated with associated periuterine varices and early opacification despite normal anterograde flow, particularly in the setting of uterine fibroids (Fig. 3).

As mentioned previously, on the basis of the current understanding of PCS, correctly detecting ovarian vein reflux is commonly considered key for the diagnosis of PCS and may be crucial for determining which patients may respond to ovarian vein ligation or embolization. Studies investigating the prevalence of ovarian vein reflux in asymp-

tomatic women using CT or static MRI on the basis of ovarian vein diameter and contrast characteristics reported a prevalence of 38–47% without correlation with angiography [6–8]. However, given the markedly lower incidence (9.9%) reported by Belenky et al. [5] in a much larger population (273 patients) using conventional venography as the gold standard, it is possible that ovarian vein reflux is frequently misdiagnosed on CT and static MRI because of the aforementioned reasons. This underscores the potential need for



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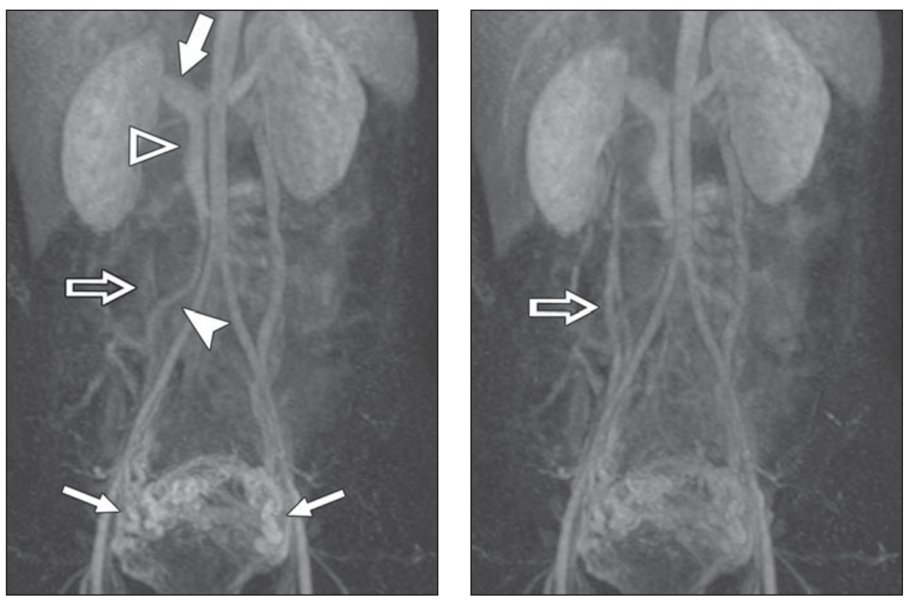

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Fig. 1—Time-resolved MR angiography in 36-year-old woman with left ovarian vein reflux and periuterine varices.
A, Coronal maximum-intensity-projection (MIP) image obtained during arterial phase. Note branches of superior mesenteric artery (*arrowhead*).
B, Coronal MIP image obtained during late arterial phase shows contrast filling of dilated left ovarian vein in retrograde fashion (*arrow*).
C, Coronal MIP image obtained during early venous phase shows prominent, fully opacified left ovarian vein (*arrow*) with filling of adjacent, parallel vein.
D, Coronal MIP image obtained during mid venous phase shows numerous tortuous periuterine varices (*thin arrows*). Note superior mesenteric vein branch (*solid arrowhead*) and superior mesenteric vein (*open arrowhead*) flowing into portal vein (*thick arrow*). Early anterograde filling of right ovarian vein is present (*open arrow*).
E, Coronal MIP image obtained during late venous phase shows increased anterograde opacification of mildly dilated and paired right ovarian vein (*arrow*). Note that given static images of **A**, **C**, **D**, or **E** alone, it is impossible to determine direction of ovarian vein flow.

TABLE 1: Sequence Parameters Used for Time-Resolved MR Angiography of Female Pelvis

Pulse Sequence	TR (ms)	TE (ms)	Flip Angle (°)	Matrix	Slices/Slab	Slice Thickness (mm)	Voxel Size (mm)	Temporal Resolution (s)
Avanto 1.5 T[a]	2.44	0.96	25	256 × 200	36–52	3	2 x 1.6 x 3	4.3
Signa HDx 1.5 T[b]	3.1	1.1	30	256 × 182	36–52	3.4	2.6 x 1.6 x 3	4.16
Tim Trio 3 T[a]	2.72	1	25	256 × 154	40	3	1.5 x 2.5 x 3	2.6

Note—For all pulse sequences, number of signals averaged, 1; field of view, 38–40 cm^2.
[a]Manufactured by Siemens Healthcare.
[b]Manufactured by GE Healthcare.

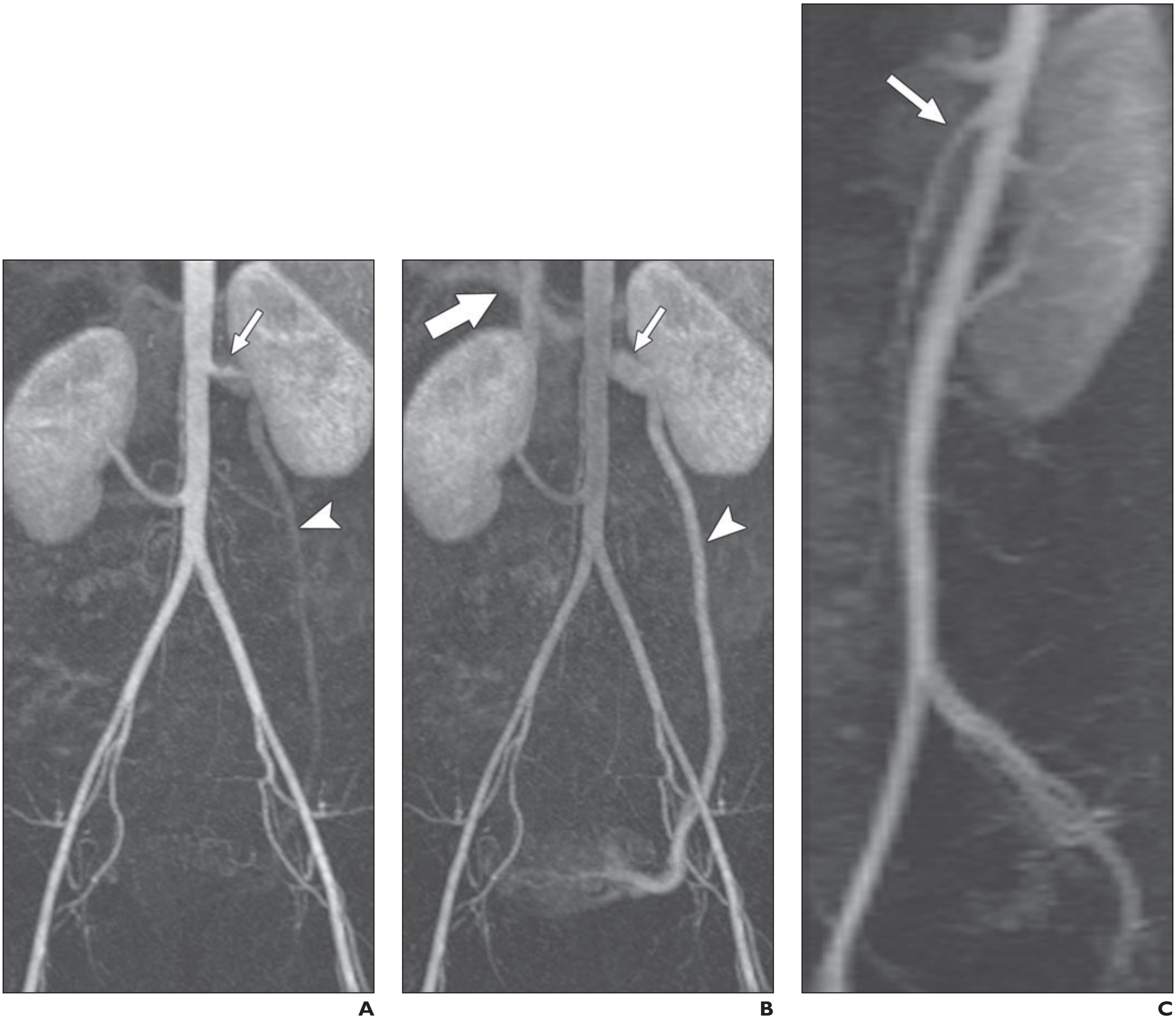

Fig. 2—Time-resolved MR angiography in 27-year-old woman with left ovarian vein reflux and possible nutcracker syndrome.
A, Coronal maximum-intensity-projection (MIP) image obtained during late arterial phase shows early reflux of left ovarian vein (*arrowhead*) with faint opacification of prominent-caliber left renal vein (*arrow*).
B, Coronal MIP image obtained during early venous phase shows increasing retrograde opacification of left ovarian vein (*arrowhead*) and left renal vein (*thin arrow*), with apparent abrupt cutoff near aorta and lack of continuity with inferior vena cava, which is compatible with compression of left renal vein between superior mesenteric artery (SMA) and aorta (nutcracker syndrome). Opacified portal vein (*thick arrow*) should not be confused with continuity of left renal vein.
C, Sagittal MIP image obtained during arterial phase shows acute 34° angle of SMA (*arrow*) with aorta, which is associated with nutcracker syndrome.

dynamic imaging. As further evidence to this effect, static MRA, when compared with conventional venography for the detection of ovarian vein reflux, shows a fairly high sensitivity of 88% but a specificity of only 67% [9].

Because TR-MRA of the ovarian veins uses only a relatively small amount of systemic contrast material administered via a peripheral IV, the hemodynamics within the ovarian vein theoretically should be unaffected. Conversely, conventional angiography requires a substantial volume of contrast material to be selectively injected into the left renal vein with a considerable velocity because of the high renal venous flow, which effectively alters the normal physiologic hemodynamics. Therefore, by artificially increasing the pressure within the left renal vein, reflux into a competent left ovarian vein may be induced, thus creating false-positive studies [16].

During conventional angiographic, CT, and sonographic examinations for detecting incompetent and dilated ovarian veins, the Valsalva maneuver and table tilting have been advocated by some to induce sufficient reflux into the ovarian veins to allow visible ovarian vein engorgement [1, 2]. As our study showed, retrograde flow through incompetent ovarian vein valves can be easily visualized in the absence of dilation when using TR-MRA. None-

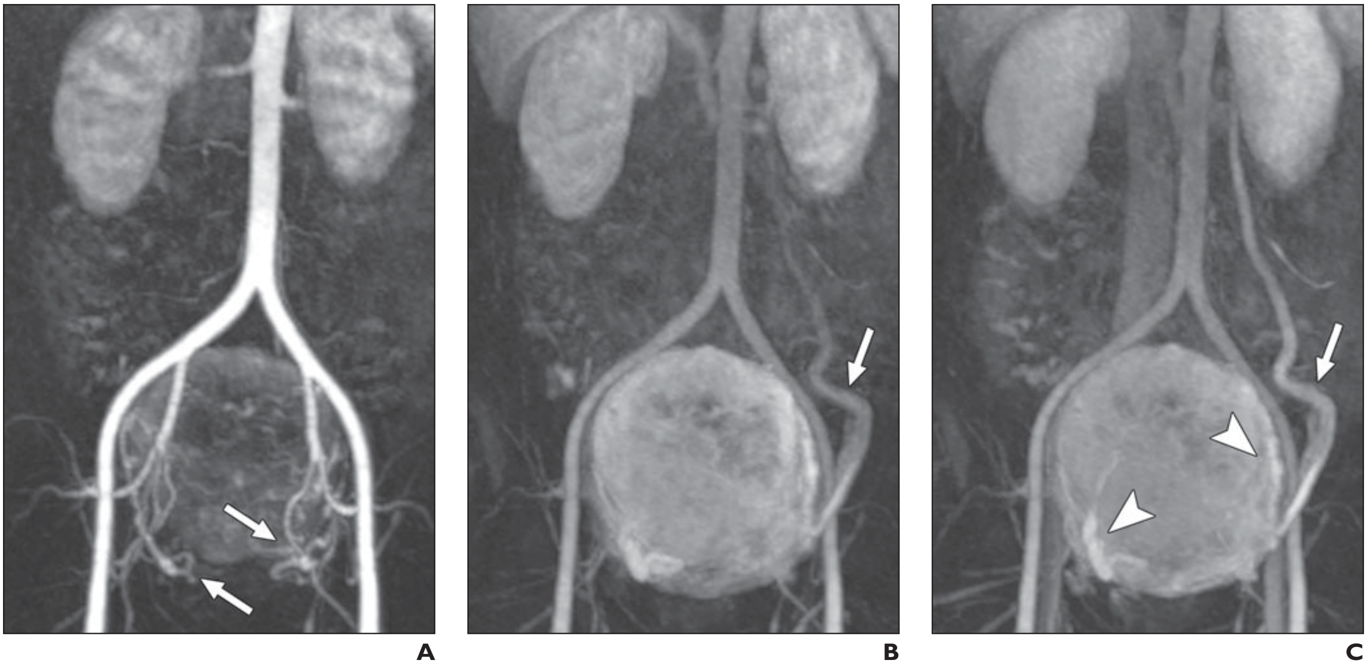

Fig. 3—Time-resolved MR angiography (TR-MRA) in 37-year-old woman with uterine leiomyoma and anterograde flow through dilated ovarian vein.
A, Coronal maximum-intensity-projection (MIP) image obtained during arterial phase shows prominent and tortuous uterine arteries (*arrows*).
B, Coronal MIP image obtained during late arterial phase shows parenchymal enhancement of uterine leiomyoma and early anterograde filling of dilated left ovarian vein (*arrow*).
C, Coronal MIP image obtained during venous phase shows continued anterograde flow via dilated left ovarian vein (*arrow*). Periuterine varices are present (*arrowheads*). Note overall similar appearance of **A** and **C** compared with Figures 1A and 1C, in which determination of direction of flow is difficult or impossible given only those images. This figure underscores utility of TR-MRA for evaluating ovarian vein reflux when compared with CT or static MR angiography imaging, even with use of multiple phases of contrast enhancement.

theless, the addition of the Valsalva maneuver to this technique may improve the sensitivity for detecting retrograde flow in the ovarian veins, particularly in cases in which reflux is very slow. However, it is theoretically possible that the Valsalva maneuver, if performed excessively, may induce reflux in otherwise competent ovarian veins.

There was significant variability in the time to visualize ovarian vein reflux after aortic opacification. The range was 7–32 seconds, with a median and mean of 15 seconds. The outlying patient with ovarian vein reflux observed at 32 seconds did not have any other vascular abnormalities to explain this slow reflux and did not have congestive heart failure. It is likely that the velocity of reflux would increase if the patient were standing. Her left ovarian vein was only mildly dilated but was quite tortuous with periuterine varices present. Clinically, she had been experiencing chronic left pelvic pain with an otherwise negative extensive diagnostic workup, including pelvic MRI, CT, ultrasound, excretory urography, barium enema, colonoscopy, stress test, and cardiac enzyme workup (for possible atypical chest pain). Therefore, she is at high suspicion for PCS and may benefit from ovarian vein ligation or embolization. Considering that the ovarian vein was not opacified until the venous phase and was only borderline dilated at 7 mm, it is quite likely that this case would have been missed with CT and static MRI.

Nutcracker syndrome, also known as left renal vein entrapment syndrome, is a known anatomic cause of ovarian vein reflux and PCS [17]. In this entity, the SMA has an abnormally acute angle with the aorta (< 60°), thereby compressing the left renal vein as it travels between

TABLE 2: Correlation of Venous Abnormalities With Symptoms of Pelvic Pain and Any Other Known Existing Pelvic Pathology That Could Produce Pain

Symptom	No.	Pain With Cause	Pain Without Cause	No Pain
Dilated ovarian vein	11	5 (45)	1 (9)	5 (45)
With ovarian vein reflux	7	3 (43)	1 (14)	3 (43)
Without ovarian vein reflux	4	2 (50)	0	2 (50)
Periuterine varices	8	4 (50)	2 (25)	2 (25)
With ovarian vein reflux	6	2 (33)	2 (33)	2 (33)
Without ovarian vein reflux	2	2 (100)	0	0
Dilated ovarian vein and varices	7	4 (57)	1 (14)	2 (29)
With ovarian vein reflux	5	2 (40)	1 (20)	2 (40)
Without ovarian vein reflux	2	2 (100)	0	0
Ovarian vein reflux	10	4 (40)	2 (20)	4 (40)
No ovarian vein reflux	90	32 (36)	2 (2)	56 (62)
All patients	100	36 (36)	4 (4)	60 (60)

Note—Data in parentheses are percentages.

the SMA and aorta, forcing venous blood return to take an alternate route to the IVC [15]. In addition to the sequelae of ovarian vein reflux, these patients also can manifest with flank pain and hematuria from resultant renal venous hypertension. Scultetus et al. [17] evaluated 51 patients with PCS and found that nine had nutcracker syndrome. In our study, of the 10 patients with left ovarian vein reflux, three were found to have imaging characteristics suggestive of nutcracker syndrome. Knowledge of this anatomic pathology is important because alternate surgical or endovascular techniques are often required to alleviate the symptoms [18].

The primary limitation of this study is that correlation with conventional angiography was not used to assess the sensitivity and specificity of TR-MRA. However, multiple studies of other vascular distributions have shown TR-MRA to be highly sensitive and specific when compared with conventional angiography [11–14]. Furthermore, TR-MRA theoretically may be more specific than conventional venography by virtue of its lack of disturbance of the normal physiologic hemodynamics in the left renal vein and ovarian veins. This study was also limited by its patient population and the relatively small number of patients with ovarian vein reflux or chronic pelvic pain. If the patient population were clinically diagnosed with PCS, then the actual utility of TR-MRA for diagnosing PCS could be analyzed. Additionally, the presence of potential PCS symptoms was determined via a retrospective review of clinical notes, which means that these symptoms were likely underreported and underestimated. Because PCS is considered an underdiagnosed condition, the clinician may not inquire or make note of potential PCS symptoms [19]. Furthermore, patients with only mild pelvic pain or patients who misattribute the pain to dysmenorrhea, for example, also likely will not even mention their symptoms to their clinician.

In conclusion, we believe that TR-MRA is a useful imaging technique for the detection of ovarian vein reflux, which may aid in evaluating PCS. This technique is potentially more sensitive than CT or static MRI because of the ability to visualize actual reflux in nondilated veins and more specific because the direction of flow can be determined easily regardless of ovarian vein dilation. Furthermore, cases of ovarian vein reflux caused by nutcracker syndrome can be detected, which may affect management options. We think that dynamic MRI could become the gold standard for the evaluation of PCS and chronic pelvic pain. Not only can MRI provide detailed anatomic information, including other possible causes of pelvic pain, but also the TR-MRA sequence can provide dynamic imaging of the pelvic vasculature, thereby replacing conventional angiography and eliminating its invasiveness and ionizing radiation. For these reasons, the TR-MRA sequence has replaced the static MRA sequence for all routine pelvic MRI studies in women at our institution.

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