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## **Interpretation of the 2021 US Edition “Single-Center Multidisciplinary Guideline for Diagnosis and Treatment of Kidney Stones During Pregnancy” : Improving Clinical Diagnostic Capability and Strengthening Multidisciplinary Collaborative Management (Postprint)**

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### **Abstract**

Renal calculi in pregnancy represent a common cause of hospitalization among pregnant patients due to non-obstetric factors, and are prone to complications such as pain, nausea, vomiting, decreased renal function, and urinary tract infections. Improper management can lead to adverse pregnancy outcomes including miscarriage and preterm birth. A U.S. medical center has collaboratively published the ‘Diagnosis and Treatment of Kidney Stones During Pregnancy - A Single-Center Multidisciplinary Guideline’ through multidisciplinary efforts, aiming to establish an evidence-based, comprehensive treatment guideline for kidney stones during pregnancy to standardize the diagnosis and management of pregnant patients with renal calculi. This guideline has formulated a total of 11 consensus statements, with 4 guiding diagnostic and imaging evaluations and 7 guiding clinical management. Notably, compared with domestic guidelines, this guideline provides evidence-based support, demonstrating the safety and efficacy of low-dose non-contrast CT during pregnancy, and recommends its prioritized use when the patient’s condition changes and the diagnosis remains uncertain. This article provides an in-depth interpretation of the aforementioned guideline.

### **Full Text**

#### **Preamble**

**Interpretation of the 2021 U.S. “Management of Nephrolithiasis in Pregnancy: Multi-Disciplinary Guidelines From an Academic Med-**

## ical Center” –Improving Clinical Diagnostic Capacity and Strengthening Multidisciplinary Collaborative Management

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### Abstract

Renal calculi during pregnancy represent a common cause of non-obstetric hospitalization among pregnant patients and are prone to complications such as pain, nausea, vomiting, declining renal function, and urinary tract infections. Improper management can lead to adverse pregnancy outcomes including miscarriage and preterm delivery. In response, a multidisciplinary team from a U.S. academic medical center jointly published the “Management of Nephrolithiasis in Pregnancy: Multi-Disciplinary Guidelines From an Academic Medical Center” to establish an evidence-based, comprehensive treatment protocol for standardizing the diagnosis and management of pregnant patients with renal calculi. This guideline formulates 11 consensus recommendations, comprising 4 for diagnostic and imaging evaluation and 7 for clinical treatment. Notably, compared with domestic guidelines, this guideline provides evidence-based support for the safety and efficacy of low-dose non-contrast CT scanning during pregnancy, which can be prioritized when the patient’s condition changes and the diagnosis remains uncertain. This article provides an in-depth interpretation of these key aspects.

**Keywords:** Nephrolithiasis in pregnancy; Diagnosis; Imaging examination; Surgical treatment; Guideline interpretation

## 1. Initial Evaluation

This section represents a key focus of the guideline, which emphasizes standardized workflows for initial patient encounters and recommends comprehensive preliminary examinations for pregnant patients with strong emphasis on collaborative management across relevant departments [Figure 1: see original paper].

**Recommendation 1:** Pregnant patients suspected of having urinary calculi should receive multidisciplinary comprehensive management, with early notification of radiology, obstetrics, and anesthesiology departments for collaborative treatment. Urology and obstetrics physicians should maintain close attention and remain on standby. During hospitalization, obstetric physicians may, based on clinical needs, advise patients on deep vein thrombosis prophylaxis (Clinical Principle).

**Recommendation 2:** Initial assessment should include inquiry into past medical history, present illness, and relevant obstetric and pregnancy history, along with comprehensive physical examination, urinalysis with urine culture, comprehensive metabolic panel, and complete blood count. Fetal monitoring should be implemented based on obstetrician recommendations (Clinical Principle).

All patients presenting with urinary calculi symptoms should undergo thorough history taking and relevant laboratory investigations. Initial laboratory tests should include complete blood count, electrolytes, urea, creatinine, uric acid, and serum calcium levels, as well as urinalysis and urine culture. If 24-hour urine metabolic evaluation is desired, it should be postponed until after delivery and weaning, as hormonal changes during pregnancy significantly affect urinary chemical composition [4].

### 1.1 Imaging Examination

**Recommendation 3:** Renal bladder ultrasound (RBUS) is the first-line imaging modality for pregnant patients suspected of having renal calculi. A high-quality ultrasound report should include assessment of renal resistive indices and ureteral jet evaluation. Additionally, transvaginal color Doppler ultrasound offers greater specificity for diagnosing distal ureteral calculi (Strong Recommendation, Evidence Level: A).

Ultrasound examination serves as the first-line adjunctive test for calculi and is particularly suitable for pregnant patients due to the absence of ionizing radiation. However, the expert panel notes significant limitations of ultrasound, including limited sensitivity for detecting obstructive renal calculi during pregnancy [5], and that simple reporting of hydronephrosis cannot reliably distinguish between obstructive urolithiasis and physiologic hydronephrosis. Resistive index (RI) [6] and ureteral jet evaluation facilitate calculi diagnosis. Furthermore, this guideline acknowledges that transvaginal ultrasound enables more precise visualization of distal ureteral calculi and may be considered when symptoms suggest distal ureteral stones, though it is theoretically contraindicated in

cases of vaginal prolapse [7].

**Recommendation 4:** If RBUS cannot confirm the diagnosis of urinary calculi and the patient's condition changes with emergence of emergency situations such as fever or hypotension, second-line imaging should be performed. In emergency circumstances, low-dose non-contrast CT scanning may be utilized (Strong Recommendation, Evidence Level: A).

In non-emergency situations, repeat ultrasound, magnetic resonance urography (MRU), or low-dose non-contrast CT may serve as alternative options. The expert panel acknowledges that each imaging modality carries its own advantages and disadvantages, requiring thorough communication with patients to make the best shared decision (Conditional Recommendation, Evidence Level C).

The 2021 edition of Chinese Urological and Andrological Disease Diagnosis and Treatment Guidelines states that urinary calculi in the second and third trimesters are more common than in the first trimester, with ultrasound as the preferred diagnostic method and MRU as an alternative. It advises against gadolinium-enhanced MRI and recommends cautious use of radiographic examinations in pregnant patients, with low-dose CT considered only as a final alternative for complex cases. However, domestic guidelines do not specify how to differentiate between routine and complex cases. In contrast, this guideline's expert panel unanimously agrees that when a pregnant patient's clinical condition deteriorates and the diagnosis remains uncertain [Figure 2: see original paper], the priority of low-dose non-contrast CT should be elevated as the next adjunctive examination following ultrasound. Although low-ionizing-radiation examinations are clinically preferable for patients, according to the American College of Obstetricians and Gynecologists (ACOG), radiation doses below 50 mGy during pregnancy are safe and do not increase the risk of pregnancy loss or fetal abnormalities [8]. Therefore, at the dose levels specified for abdominal/pelvic CT imaging (<50 mGy), the risks of fetal malformation and cognitive impairment are extremely low [9]. The American College of Radiology (ACR) and ACOG recommend that low-dose non-contrast CT, with its lower ionizing radiation side effects, may be used when necessary to assist clinical evaluation. Additionally, the expert panel considers MRI to have poor sensitivity for calculi, is less convenient and rapid than CT, and theoretically poses risks of fetal hearing damage and tissue heating, so MRI should be avoided during the first trimester.

## 2. Treatment

**Recommendation 5:** If the patient's clinical symptoms can be controlled with medication and no complicating factors are present, continued trial of medical expulsive therapy and analgesia is appropriate. Patients who fail to pass calculi with medical therapy should discuss ureteroscopy with their follow-up urologist (Strong Recommendation, Evidence Level: B).

The guideline indicates that conservative management is a reasonable option

for stable patients with controllable symptoms, as 50%-80% of urinary calculi pass spontaneously during pregnancy [10,11]. Selective alpha-blockers are Category B drugs in pregnancy and can be used safely, with a retrospective study confirming the safety of tamsulosin-assisted stone passage in pregnant women, demonstrating no significant differences in maternal and fetal outcomes [12]. Medical expulsive therapy is therefore reasonably safe.

As noted in the guideline, pregnant women have higher spontaneous stone passage rates than the general population (81% vs. 47%) due to progesterone-induced smooth muscle relaxation and ureteral dilation [13,14]. Domestic guidelines even suggest that approximately 90% of pregnant patients can pass calculi spontaneously. However, Mayo Clinic clinical studies indicate that the actual spontaneous passage rate for urolithiasis during pregnancy is much lower than reported data, at only 48% [15] (43 of 90 patients). This guideline does not introduce or recommend spontaneous passage as a treatment strategy, possibly due to questionable data on actual spontaneous passage rates during pregnancy. The EAU 2022 edition of stone treatment guidelines further recommends continuous ultrasound monitoring throughout pregnancy until delivery, regardless of whether conservative or surgical intervention is chosen.

In addition to tamsulosin, increasing urine flow to promote stone passage is also safe. Analgesic selection requires caution in pregnant patients with calculi. NSAIDs, suitable for analgesia in non-pregnant populations with normal renal function, carry risks of adverse fetal renal effects, oligohydramnios, and premature ductus arteriosus closure, and are generally avoided during pregnancy. Codeine has also been shown to cause significant side effects in early pregnancy [16], such as neonatal withdrawal symptoms. Opioids such as meperidine are typically selected for pregnant patients with pain [17].

Although the guideline expert panel recommends medical expulsive therapy and discusses tamsulosin use, both the alpha-adrenergic receptor blocker tamsulosin and the calcium channel blocker nifedipine are commonly used expulsive agents that can assist spontaneous stone passage in the general population. Nifedipine, frequently used for hypertension in pregnancy, represents another option. However, more rigorous clinical evidence is needed to support drug selection, and clinicians should fully inform patients that the therapeutic and adverse effects of these medications for pregnant patients with calculi remain under investigation.

Most calculi patients develop concurrent urinary tract infections, and pregnant women are no exception. The guideline does not specifically address antibiotic use for calculi complicated by urinary tract infection during pregnancy. Enterobacteriaceae are the most common pathogens in urinary tract infections. Based on long-term observations, pregnancy-safe antibiotics include cephalosporins, penicillins, macrolides, and nitrofurantoin, which can serve as primary treatment options for urinary tract infections in pregnant patients with calculi, though specific drug selection should be based on urine culture results and microbiology specialist recommendations [18].

**Recommendation 6:** If septic obstructive calculi are suspected, renal decompression via ureteral stent placement is recommended regardless of gestational age. Furthermore, due to mechanical changes from the gravid uterus and progesterone effects—including impaired gastric motility and lower esophageal sphincter tone, combined with positional influences—there exists aspiration risk. Therefore, transurethral ureteral stent placement is preferred over percutaneous nephrostomy [Figure 3: see original paper] (Expert Opinion).

Patients requiring intraoperative fetal monitoring after obstetric consultation should undergo ureteral stent placement with collaborative involvement from anesthesiology, obstetrics, and neonatology specialists (Clinical Principle).

For patients with prior urinary reconstruction history (such as neobladder or transplanted kidney) or calculi large enough to require percutaneous nephrolithotomy, ultrasound-guided percutaneous nephrostomy (PCN) should be the first choice. Preoperative preparation should include readiness for both transurethral ureteral stent placement and PCN, allowing direct conversion to PCN if natural tract access fails (Expert Opinion).

Beyond urology, obstetricians should determine the need for intraoperative fetal monitoring, obtain informed consent for emergency cesarean section when possible, arrange delivery equipment, and notify the neonatal intensive care unit (Expert Opinion).

**Recommendation 7:** Following transurethral ureteral stent placement, the stent should be changed every 4 weeks until definitive management is performed (Strong Recommendation, Evidence Level C).

Regarding these two surgical drainage approaches, the guideline expert panel believes no high-quality evidence demonstrates the superiority of one method over the other [19]. However, a retrospective study of 3,904 pregnant patients with renal calculi reported preterm delivery rates of 19.6% for PCN, 11.2% for ureteroscopic surgery, and 9.1% for conservative management [20]. Therefore, out of caution, the panel recommends ureteral stent placement as the first-choice surgical drainage for pregnant patients with renal calculi. In reality, regardless of drainage method, pregnant women's metabolic changes lead to hyperuricemia and hypercalciuria, causing crystalline deposition on ureteral stent surfaces and increasing the difficulty of subsequent secondary procedures. Regular follow-up is essential to ensure timely removal, with stent changes recommended every 4 weeks during indwelling periods.

When calculi cause obstruction, the options are limited to indwelling ureteral stents or external nephrostomy tubes, each with distinct advantages and disadvantages. Selection depends on current clinical conditions, medical resources, and physician and patient preferences, with each approach carrying risks of infection, tube displacement, or obstruction. The stent change interval lacks standardization, with clinical practice defaulting to 4-8 weeks [21]. Comparatively, ureteral stents are preferred due to the absence of external tubing, making care more convenient and safe, though stents can cause bothersome bladder irrita-

tive symptoms. Septic patients should typically receive PCN as the first choice to avoid excessive ureteral manipulation [22]. For nephrostomy tube care, specialists recommend regular irrigation [23]. Shalom J [24] et al. proposed that urinary calculi occurring before 22 weeks gestation may preferentially receive PCN, while ureteral stent placement may be selected later in pregnancy [25], with nephrostomy tube changes every 6-8 weeks. However, these recommendations are based on individual clinicians' experiences and require further clinical data validation.

**Recommendation 8:** If conservative management fails, ureteroscopy should be considered first-line treatment in non-special circumstances (special circumstances illustrated in Figure 3) (Strong Recommendation, Evidence Level B).

**Recommendation 9:** The expert panel recommends neuraxial anesthesia (spinal, epidural, or combined spinal-epidural) as the preferred choice for obstetric patients because physiological changes during pregnancy increase aspiration risk and airway management difficulty, while neuraxial anesthesia also minimizes fetal exposure to anesthetic agents. The guideline suggests that when selecting any type of anesthetic, the possibility of difficult airway management and aspiration should be fully considered and anticipated (Moderate Recommendation, Evidence Level B).

The expert panel considers ureteroscopy safe, capable of resolving calculi in a single procedure, theoretically reducing anesthetic and fetal exposure, and potentially avoiding indwelling catheters if urine is not infected. Multiple studies confirm that ureteroscopy during pregnancy is safe and appropriate, with postoperative complication rates comparable to non-obstetric patients [26-28]. In comparison, 42.1% of patients undergoing ureteral stent placement required early induction at 38 weeks gestation, and 10.9% experienced preterm delivery within 24 hours post-procedure [29]. This perspective aligns with domestic treatment guidelines, though this guideline does not address whether ureteral stents should be placed post-ureteroscopy or the duration of stenting. According to the 2021 edition of Chinese Urological and Andrological Disease Diagnosis and Treatment Guidelines, ureteroscopic lithotripsy is safe and effective [30], with a single-session stone-free rate of 91%, recommending postoperative ureteral stent placement for over 72 hours to relieve pain, fever, and other symptoms caused by obstructive calculi. The guideline recommends ureteroscopy for patients failing conservative management but does not discuss laser fibers required for lithotripsy; literature review indicates holmium laser [31-33] is suitable for pregnant patients with renal calculi.

**Recommendation 10:** When conditions permit, neuraxial anesthesia (spinal, epidural, or combined spinal-epidural) should be the first choice because physiological changes during pregnancy increase aspiration incidence and airway management difficulty, while neuraxial anesthesia also reduces fetal exposure to anesthetic agents and drugs. However, general anesthesia may also be selected when necessary, as no definitive evidence indicates greater fetal harm from general anesthesia. When planning any anesthetic approach, the possi-

bility of difficult airway management and aspiration should be fully considered and anticipated (Moderate Recommendation, Evidence Level B).

The ACOG Committee Opinion on non-obstetric surgery during pregnancy states, “No evidence demonstrates that anesthetic use during pregnancy increases teratogenic or fetal harm risk” [34]. Based on this, the expert panel believes both general and regional (spinal, epidural, and combined spinal-epidural) anesthesia can be safely administered during pregnancy. However, physiological changes in respiratory and gastrointestinal systems during pregnancy increase risks of difficult airway management and aspiration. Therefore, when feasible, local anesthesia for ureteral stent placement should be prioritized during pregnancy. More importantly, hemodynamic and oxygen saturation monitoring must be maintained throughout anesthesia to avoid hypotension, hypoxia, hypercapnia, and hypocapnia. Maternal hypoxia can lead to uteroplacental insufficiency, resulting in fetal hypoxemia and acidosis, while volatile anesthetics reduce uterine activity, with fetal monitoring available when necessary. Anesthetic selection for surgical procedures should be individualized—for example, septic shock represents a contraindication for regional anesthesia, making emergency PCN placement under local anesthesia or conscious sedation an alternative option.

**Recommendation 11:** Urology and obstetrics physicians should regularly follow up with patients who have indwelling ureteral stents or nephrostomy tubes and recommend definitive ureteroscopic treatment (Expert Opinion).

### 3. Summary

This article represents the first domestic and international guideline treating nephrolithiasis in pregnancy as an independent disease entity, simplifying previous clinical treatment workflows and emphasizing hospital multidisciplinary collaboration and comprehensive patient management. From an evidence-based medicine perspective, the guideline confirms the safety and diagnostic accuracy of low-dose CT compared to RBUS. Additionally, for patients with obstructive renal calculi, the guideline recommends prioritizing ureteral stent placement. However, the recommendations are limited to pregnancy-related renal calculi treatment and do not deeply explore management of calculi complications or discuss selection of laser fibers for ureteroscopy. Due to insufficient evidence-based medical evidence, this guideline has limitations, and clinicians should still develop individualized diagnosis and treatment plans based on patients’ clinical realities and existing guideline recommendations to achieve optimal clinical outcomes.

**Conflict of Interest:** None.

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