Diagnostic accuracy of ultrasound versus fluoroscopy for detecting residual fragments during retrograde intrarenal surgery: a randomized controlled trial

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PROJECT SUMMARY:

Ultrasound is currently gaining popularity as an alternative imaging modality for the diagnosis and treatment of urolithiasis. However, the benefit of ultrasound on the diagnostic accuracy of detecting residual fragments during retrograde intrarenal surgery (RIRS) has never been evaluated in a randomized study. Its use would reduce radiation exposure for patients and care team members as well as improve stone free clearance rates for surgery. Therefore, we plan to conduct a randomized trial to assess the diagnostic accuracy of ultrasound and fluoroscopy in conjunction with endoscopic examination for detecting residual stone fragments during retrograde intrarenal surgery. After admission, approximately 172 subjects will be randomized in a 1:1 ratio to receive ultrasound or fluoroscopy before completing RIRS. Subsequently, four weeks after the operation, we will compare with routine low-dose non-contrast computed tomography as a gold standard for detecting residual fragments. If ultrasound is more accurate than fluoroscopy in detecting residual fragments, we will encourage this approach as it can reduce radiation exposure for patients and healthcare professionals.

HYPOTHESIS:

The diagnostic accuracy of ultrasound in conjunction with endoscopic examination for detecting residual stone fragments during retrograde intrarenal surgery will be superior to fluoroscopy.

AIMS:

Primary outcome: To measure the diagnostic accuracy of ultrasound and fluoroscopy in conjunction with endoscopic examination for detecting residual fragments during retrograde intrarenal surgery for renal stones treatment.

Secondary outcome: To measure the sensitivity, specificity, positive predictive value and negative predictive value of ultrasound and fluoroscopy in conjunction with endoscopic examination for detecting residual fragments during retrograde intrarenal surgery for renal stones treatment.

DESIGN:

We plan to conduct a prospective single-center, randomized controlled trial to assess the diagnostic accuracy of ultrasound and fluoroscopy in conjunction with endoscopic examination for detecting residual stone fragments during retrograde intrarenal surgery. After admission, approximately 172 subjects will be randomized in a 1:1 ratio to receive ultrasound or fluoroscopy before completing RIRS. Subsequently, four weeks after the operation, we will compare with routine low-dose non-contrast computed tomography as a gold standard for detecting residual fragments.

BACKGROUND AND SIGNIFICANCE:

Retrograde intrarenal surgery (RIRS) has become more established and has played an increasingly important role in treating kidney stones since advancements in endoscopic and equipment technology[1,2]. However, although RIRS has a higher stone-free rate than in the past, the residual fragments remain a major issue, whether they cause pain, obstruction, or require additional procedures[3]. Therefore, in addition to a thorough endoscopic examination, it is crucial to have a reliable approach for detecting residual fragments[4].

Fluoroscopy is a traditional method used in conjunction with endoscopic examination. However, the main drawbacks are radiation exposure, poorly visible radiolucent stones, and small stones concealed by bowel gas[5]. Nowadays, ultrasound has demonstrated effectiveness as an alternate imaging modality for the diagnosis and treatment of urolithiasis[6]. Previous reports have shown that ultrasound-guided ureteroscopy is a safe and efficient method for treating urinary stones in pregnant women and children without ionizing radiation[7,8]. In terms of kidney stone detection, it is also helpful in detecting radiolucent stones, determining their anatomical location inside the kidneys, and monitoring any complications that may arise during the procedure[6]. However, no studies have been found to date assessing the advantages in diagnostic accuracy of this method. Thus, we will conduct a randomized trial to compare the diagnostic accuracy of ultrasound and fluoroscopy in conjunction with endoscopic examination for detecting residual fragments during RIRS to postoperative low-dose non-contrast computed tomography (NCCT), which is considered the gold standard for diagnosing kidney stones.

PRELIMINARY STUDIES:

We looked for literature related to the diagnostic accuracy of ultrasound and X-ray in the diagnosis of kidney stones and their limitations, which has a variety of information as shown.

Ray et al. (2010)[9] published a systematic review of **ultrasound** for the detection of urinary tract calculi, which found that it had a sensitivity and specificity of **45%** and **88%** for renal calculi, respectively. Sensitivity is reduced for stones < 3 mm, which might not produce a shadow, and stones can be missed in a decompressed system due to the difficulty in distinguishing echogenic stones from echogenic central sinus fat in the kidney.

Kanno et al. (2017)[10] compared the efficacy of plain KUB and ultrasound to NCCT on the same day for the detection of urinary tract stones in 822 patients. **Ultrasound** had a sensitivity of **88.7%**, a specificity of **68.3%,** a PPV of 81.1%, and a NPV of 80.0%. **Plain KUB** had a sensitivity of **49.1%,** a specificity of **99.1%,** a PPV of 98.8%, and a NPV of 56.0%. For the **combination** of the two modalities, it had a sensitivity of **89.9%,** a specificity of **68.2%,** a PPV of 81.2%, and a NPV of 81.6%. Plain KUB had a low detection rate for stones smaller than 5 millimeters.

Roberson et al. (2018)[11] reported the diagnostic performance of ultrasound for nephrolithiasis in 69 children compared to NCCT within 24 hours. **Ultrasound** had a sensitivity of **66.7%,** a specificity of **97.4%,** a positive predictive value (PPV) of 95.2%, and a negative predictive value (NPV) of 79.2% for detecting nephrolithiasis in any kidney. In patients with a documented history of nephrolithiasis (n = 14), ultrasound had a sensitivity of **80.0%,** a specificity of **100%,** a PPV of 100%, and a NPV of 66.7%.

Danilovic et al. (2018)[4] reported the most suitable approach to assess residual stone fragments after RIRS in 115 renal units by endoscopic examination at the end of the procedure and by ultrasound and kidneys ureters bladder radiography (KUB) on the 90th postoperative day compared to NCCT which is considered the gold standard. They found that sensitivity for **endoscopic examination** of kidney stones **(traditionally performed with fluoroscopy), ultrasound** and **KUB** were **89.7%, 89.7%,** and **20.6%,** respectively. The specificity were **46.5%, 74.4%** and **100%** respectively. The **accuracy** were **57.4%, 78.3%** and **80%**. Neither ultrasound nor KUB identified residual fragments between 0 – 2 mm. Ultrasound misdiagnosed stone-free as residual fragments > 2 mm in 25.6%. However, if ultrasound was stone-free, the result was correct in 95.5%. If the endoscopic evaluation described residual fragments > 2 mm, ultrasound was correct in all cases. KUB alone had only 31.6% sensitivity to detect residual fragments > 2 mm and it was not able to add sensitivity or specificity to ultrasound. They suggested that If an endoscopic examination

reveals residual fragments < 2 mm, NCCT should be performed on the 90th postoperative day. Ultrasound is enough if endoscopic evaluation shows residual fragments > 2 mm.

From the literature, Danilovic et al. whose that endoscopic examination, ultrasound, and plain KUB (plain KUB is comparable to fluoroscopy) were used to examine kidney stone fragments. They found that ultrasound alone showed similar sensitivity and higher specificity than endoscopic examination. They also found that plain KUB, like ultrasound, couldn't find stone pieces smaller than 2 mm. In addition, stone fragments that are less than 4 mm usually don't cause significant problems for patients. We therefore think it is reasonable to propose that our research protocol where we are combining ultrasound with endoscopy versus fluoroscopy plus endoscopy, puts us in a space of equipoise, where both modalities are similar in efficacy and accuracy. And in current state, people use ultrasound + endoscopy for special situations like kids and pregnant people, so we aren't performing anything outside of standard of care with our ultrasound protocol. We're just applying currently common practice that's done in special populations to a broader population of patients.

PROCEDURES / METHODS:

Well-informed consent will be obtained from every patient after giving balanced information about options of both ultrasound and fluoroscopy before enrollment in the trial. We confirm that the RIRS procedure will be performed in accordance with usual care and assignment to the ultrasound group will not affect how this procedure is performed because we routinely perform ureteroscopy with ultrasound guidance in pregnancy patients, for example, as well as in children. Demographic data and stone characteristics determined by low-dose NCCT will be collected in all patients preoperatively. Randomization was carried out preoperatively using computerized random numbers. Patients will be allocated preoperatively by sealed envelope technique to standard fluoroscopic (control) or ultrasound (test) as the primary imaging methods. All RIRS procedures will be performed by a member of our endourological staffs. Before completing the procedure, a complete endoscopic examination will be performed in conjunction with fluoroscopy or ultrasound (as the randomization, regardless of the size of the residual stone) by the same endourologist to determine the size of the largest residual fragment, categorizing them as stone free, ≤ 2 mm, and >2 mm. All patients will undergo routine low-dose NCCT or Ultrasound imaging at four weeks as part of routine clinical care to assess for residual fragments. A low-dose NCCT or Ultrasound will be evaluated by a radiologist blinded to surgery and intraoperative imaging, categorizing them as stone free, ≤ 2 mm, and >2 mm. Residual fragments will be defined as stone fragments of a size greater than 0 mm. Surgical complications will be categorized according to the modified Clavien-Dindo classification[12].

STATISTICAL METHODS:

- Demographic data, stone characteristics, operative time, and postoperative complications, will be presented as frequencies and percentages for categorical variables, and as mean ± SD or median and interquartile ranges for continuous variables.
- The results for both groups in comparison to the low-dose NCCT will be entered into a 2×2 contingency table from which the accuracy, sensitivity, specificity, and predictive values will be determined. A 95% CI will be calculated for the accuracy, sensitivity, specificity, and predictive values. The Chi-square test will be used to compare the diagnostic accuracy of each arm.
- A two-sided p-value of less than 0.05 is considered a statistically significant difference.

SAMPLE SIZE AND ELIGIBILITY CRITERIA

ENROLLMENT TARGET: N = 172

SAMPLE SIZE JUSTIFICATION:

The sample size is calculated with a power of 80% and a two-sided alpha level of 0.05 to detect a 20.9% difference in the accuracy of detecting residual fragments between endoscopic examination in conjunction with fluoroscopy and ultrasound[4]. Given an anticipated dropout rate of 10%, Therefore, approximately 86 patients will be required in each group, for a total of 172, on the basis of an expected recruitment of 15 patients per month over a period of 12 months.

INCLUSION CRITERIA:

- Patients over the age of 18.
- Consecutive patients with a diagnosis of renal stone or ureteral stone with a plan to undergoing RIRS for stone removal.

EXCLUSION CRITERIA:

- Patients who decline informed consent.
- Pregnancy
- Kidney transplantation
- Ectopic kidney
- Patients undergoing concurrent bilateral stone removal surgery.
- Patients whose pain cannot be controlled when presenting at the Emergency Department.

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Mock Table 1 Demographic, stone characteristics and perioperative data of patients in fluoroscopy and ultrasound groups.

Variable	Total n = xx	Fluoroscopy n = xx	Ultrasound n = xx
Gender (%)			
− Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Age (years, mean ± SD)	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x
BMI (kg/m^2, mean ± SD)	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x
Laterality (%)			
− Right	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Left	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stone size (mm, mean ± SD)	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x
Density (HU, mean ± SD)	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x
Location (%)			
− Upper calyx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Mid calyx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Lower calyx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Renal pelvis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Staghorn	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Multiple	Xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Diverticular stone	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Operative time (mins, mean ± SD)	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x
Complication (%)			
− Clavien Dindo I	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Clavien Dindo II	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Clavien Dindo IIIa	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
− Clavien Dindo IIIb	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Variable	Total n = xx	Fluoroscopy n = xx	Ultrasound n = xx
− Clavien Dindo IV	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Mock Table 2 Comparison between fluoroscopy and ultrasound to low-dose non-contrast computed tomography for detecting residual fragments.

Method		Low-dose NCCT			Total
		Stone free	0-2 mm	>2 mm	
Fluoroscopy	Stone free	xx	xx	xx	xx
	≤2 mm	xx	xx	xx	xx
	>2 mm	xx	xx	xx	xx
Ultrasound	Stone free	xx	xx	xx	xx
	≤2 mm	xx	xx	xx	xx
	>2 mm	xx	xx	xx	xx
Total		xx	xx	xx	xx

NCCT: non-contrast computed tomography

Mock Table 3 Diagnostic accuracy of ultrasound versus fluoroscopy for detecting residual fragments during retrograde intrarenal surgery.

	Ultrasound	Fluoroscopy	Difference	*P*-value
Accuracy	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	x.xx
Sensitivity	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	x.xx
Specificity	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	x.xx
PPV	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	x.xx
NPV	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	xx.x% (95%CI xx.x% - xx.x%)	x.xx

PPV: positive predictive value
NPV: negative predictive value