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Diagnostic Accuracy of Low and Ultra-Low Dose CT for Identification of Urinary Tract Stones: A Systematic Review

Keywords

Stones · Computed tomography · Urolithiasis · Non-contrasted computed tomography scan of the kidney, ureter, and bladder · Radiation safety · Renal colic

Abstract

Background: Non-contrast computed tomography of the kidneys, ureters, and bladder (CT KUB) is the investigation of choice for renal colic; however, radiation exposure can be a concern. ***Aims:*** The study aimed to investigate the diagnostic accuracy of low dose (LD) and ultra-low dose (ULD) CT of the urinary tract for detection of urinary tract stones in patients with renal colic. ***Methods:*** A Cochrane style systematic review of the literature from 1995 to 2017 was carried out. Literature search and data extraction were conducted by 2 reviewers. Specificity and sensitivity values were calculated for LD (<3.5 mean radiation dose [mSv]) and ULD (<1.9 mSv) CT separately. ***Results:*** A total of 12 studies were included following screening. A total of 1,529 patients were included in the review (475 in the LD group and 1,054 in the ULD group). Using standard dose CT KUB as the reference standard, the sensitivity of LD CT KUB ranged from 90 to 98% and specificity from 88 to 100%. The sensitivity of ULD CT KUB ranged from 72 to 99% and the specificity ranged from 86 to 100%. The diagnostic accuracy for LD CT was 94.3% and for ULD CT was 95.5%. ***Conclusions:*** LD and ULD CT KUB provide effective methods of identifying urinary tract stones. High diagnostic accuracy, sensitivity, and specificity are maintained despite significant radiation dose reduction in comparison to standard dose CT.

Introduction

Renal colic is a common condition affecting 1 in 1,000 people per year [1]. A non-contrasted computed tomography scan of the kidney, ureter, and bladder (CT KUB) is generally the imaging investigation of choice for patients with a suspected diagnosis of urinary tract stones and is recommended by the European Association of Urology and the American Urological Association [2, 3]. CT KUB has the ability to not only detect stones but to determine their size, number, and location. This cannot be replicated with X-ray or ultrasound.

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Renal colic affects all ages, with the first stone often arising for men in their 20s and peak incidence between 40 and 60 years [4]. Women are affected at a younger age and have peak onset in their late 20s [4]. Urolithiasis is also associated with recurrence rates of 50–70% at 10 years [5]. Therefore, patients are likely to be subjected to repeated imaging. Though 40–60% of stones are visible on plain KUB x-rays, CT KUBs will invariably be required if treatment is planned, in addition to the 40–60% of patients where the stone is not visible on KUB X-ray.

Given the radiation dose associated with CT KUB, the use of repeated CT scans has been an area of concern. The UK National Dose Reference Level for CT scans of the abdomen and pelvis for KUB examinations assessing stones/colic is 745 mGy cm. This equates to an effective dose of 6.44 mean radiation dose (mSv), based upon a conversion factor of 0.014 mSv/mGy as per ICRP 103 from 2008 [6]. Lifetime radiation doses of 100 mSv are associated with a 1 in 200 risk of developing a radiation-related cancer [7]. To address this, many studies have described reduced dose CT KUB protocols for stone detection. Some report radiation doses comparable with abdominal X-ray KUB [8]. Dosages vary from those considered to be a low dose (LD) CT KUB (with doses <3.5 mSv) to ultra-low dose (ULD) CT KUB (with doses <1.9 mSv). Typically, the radiation dose for a CT KUB will be a function of the kilovoltage used (kVp), the tube current applied (mAs), and the extent of coverage included. These factors all combine to produce a dose-length product (DLP) which is recorded for each scan with units of mGy cm, that is, the radiation in mGy multiplied by the scan length in cm. For any given scan, an estimate of the radiation dose that has been applied can be approximated by multiplying this DLP value by a conversion factor specific to the region imaged, in this case the abdomen and pelvis. This conversion factor takes into account tissue weighting factors related to the organs at risk in the body regions concerned. These weighting factors were changed in ICRP 103 published in 2008 [9] and this is of some relevance when reviewing the literature.

With radiation dose reduction, there is usually the penalty of an associated increase in image noise and resulting in potential reduction of sensitivity and specificity. There are several approaches to reducing CT dose. In general, the earlier studies of LD scanning employed techniques that reduce kVp and/or mAs where image reconstruction from raw data is performed using traditional filtered back projection (FBP). Reducing slice thickness has been shown to improve the ability to pick up small urinary calculi; however, this too is hampered by an associated increase in image noise [10]. This is particularly apparent in LD scans where mA and kVp have been significantly reduced [11]. The step change to allow ULD scanning has largely been engendered by the move to the use of various iterative reconstruction (IR) methods which are much more computationally intensive and have only more recently become available clinically. IR techniques can be used to reconstruct an image acquired in thin sections into an image with reduced noise equivalent to thicker sections, that is, images with less noise than FBP at any given radiation dose and slice thickness [12]. Hence, final images with image noise equivalent to FBP can be obtained by using IR to reconstruct images from raw data that were acquired at lower dose. However, the images produced may be qualitatively different to FBP which may impact upon sensitivity/specificity.

With the drive to reduce dose there has also been recognition that the extent of coverage is a significant influence. Limiting coverage to the area where the stones are expected also significantly impacts dose but may limit the scope for making alternative diagnoses, one of the strengths of CT KUB imaging in the setting of primary diagnosis. However, this is of course less relevant for follow-up examinations.

Our primary aim was to investigate the diagnostic accuracy of these reduced dose scans for stone detection in patients with renal colic and evaluate how these compared to the reference standard. Several new studies have since been published investigating the use of LD CT KUB for urolithiasis [13, 14]. However, we have conducted a systematic review and diagnostic accuracy meta-analysis of papers concerning LD and ULD CT KUB and are the only group publishing diagnostic accuracy data sub-analyzed for LD and ULD CT KUB separately.

Methods

Search Strategy and Study Selection

The systematic review and meta-analysis was performed according to the Cochrane diagnostic accuracy review guidelines [15].

A literature search was performed in August 2017 of the following databases: MEDLINE (1990–2017), EMBASE (1990–2017), Cochrane Central Register of Controlled Trials – CENTRAL (in The Cochrane Library – Issue 1, 20161), and the following search platforms: Google Scholar, PubMed, and individual urological journals. No limitations were placed on language, region, or publication type.

The following search terms were utilised: stones, calculi, urolithiasis, urinary calculi, renal colic, CT, CT KUB, LD, ULD, and radiation. These were combined with Boolean operators (AND, OR) to gain results.

Medical Subject Heading [MESH] phrases included: (["Calculi" OR "Urinary Calculi"] OR "Urolithiasis") AND ("Tomography, X-Ray Computed") (["Calculi" OR "Urinary Calculi"] OR "Urolithiasis") AND ("Colic" OR "Renal Colic").

Inclusion/Exclusion Criteria

We included all studies that compared LD or ULD CT for the detection of urinary tract stones compared to a reference standard. We defined a reference standard as either a standard dose CT KUB or physical stone finding (e.g., as seen in ureteroscopy). In accordance with the accepted and agreed definitions, we defined LD as <3.5 mSv and ULD as <1.9 mSv [13]. All languages were included. Where data were not reported in a true positive (TP), true negative (TN), false positive (FP), and false negatives (FN) format, corresponding authors of these relevant studies were contacted and if data were provided, the study was included [16]. Where data were not extractable and/or corresponding authors did not respond, the study was excluded. Any study that did not use a reference standard was excluded [17–23].

Data Extraction and Analysis

Data extraction was carried out by 2 independent reviewers (F.R. and O.M.A). The following variables were extracted from studies that met the inclusion criteria: study demographics, patient demographics, and diagnostic accuracy figures – TP, TN, FP, and FN. Where the study reported in this format, a pooled diagnostic accuracy was calculated. Summary receiver operating characteristic curves (SROC) were constructed using the random effects DerSimonian-Laird model. We used Review Manager (RevMan 5.3) for all statistical analyses.

Quality Assessment

The methodological quality of the included studies was assessed independently by 2 authors (F.R. and O.M.A.) using the QUADAS-2 assessment tool. Our study results were then reported in accordance with the STARD guideline [15, 24].

Results

Initial search of the literature yielded 3,596 studies. Titles review led to exclusion of 3,379 papers as these were not directly relevant to the research question. Review of the abstracts led to exclusion of 185 papers due to inappropriate study population or comparator investigation. Finally, 32 relevant papers were identified for more detailed review. Of these, 25 studies from the literature search were found to fit our inclusion criteria and 13 of these papers either did not publish TP, TN, FP, FN numbers or they reported their results based on "per stone" analyses rather than "per patient". In these cases, we made attempts to communicate with the publishing author to request access to the TP/TN/FP/FN data per patient. This resulted in 12 articles for inclusion in the review [8, 16, 25–34]. Flow chart shown in Figure 1.

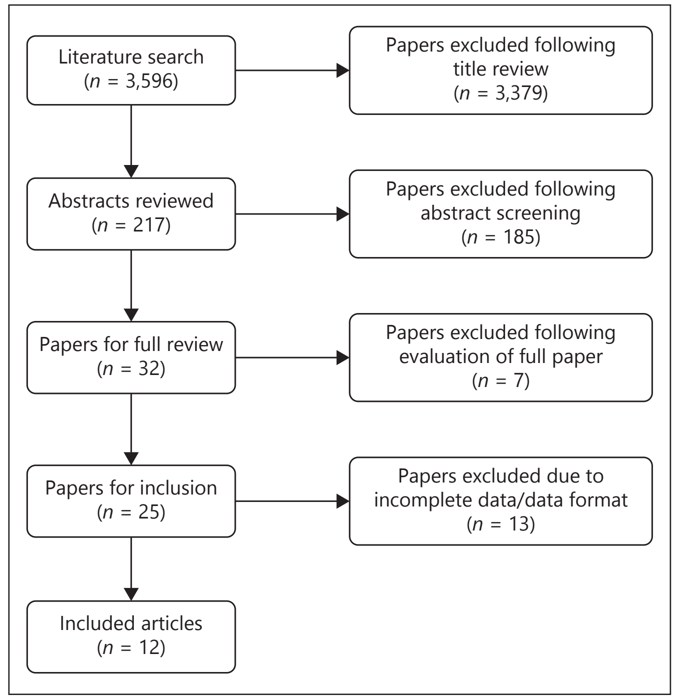

Fig. 1. Flow chart of literature search.

Characteristics of the Included Studies

The final 12 studies were published between 2001 and 2015. Studies originated from Germany, South Korea, Belgium, Switzerland, France, China, UK, USA, and Kenya. They included a total of 1,439 patients. Baseline characteristics are shown in Tables 1 and 2. All the studies compared reduced dose CT KUB to standard dose CT KUB or other standard imaging, for example, CT intravenous urogram (IVU). Studies were separated into LD and ULD CT groups, based on the mean radiation dose (mSv). Of these, 4 studies assessed LD CT KUB, including a total of 475 patients [25–28] and 8 studies looked at ULD CT KUB including a total of 1,054 patients [8, 16, 29–34]. Also, 2 of the studies in this category reported TP/TN/FP/FN data from multiple scan reviewers. In these cases, each of the scan reviewers was considered as a separate data set.

Definitions of Reference Standard Test

The index test was LD CT KUB in 4 papers [25–28] and ULD CT KUB in 8 papers [8, 16, 29–34]. There was variation in the reference standards used, with 7 papers using standard dose CT KUB as the reference standard [8, 16, 25, 27, 30, 32, 34]. Of the remaining studies, 1 used CT intravenous urography as their reference standard [26] and 3 used physical stone demonstration either during

Table 1. Baseline characteristics for LD CT studies (mean radiation 2.1–4.5 mSv)

Study (ref.)	Country	Year	Number of patients	Age, range (mean)	Gender (M:F)	mSv	CT specifications	Dose reduction methods	Reference standard
Meagher et al. [26]	UK	2001	69	18–78 (42.3)	55:14	3.5	4 detector row scanners, 5 mm slice thickness	Reduced mAs	CTIVU
Twahirwa et al. [28]	Kenya	2009	104	17–79 (40)	47:43	Not reported	16 detector row scanner, 1.25 mm slice thickness	Reduced mAs	Surgical retrieval, presence at ESWL, Clinical and imaging follow-up
Fracchia et al. [27]	America	2012	101	21–82 (53.4)	70:31	2.1	'Standard software 64 slice CT scanner ', Slice thickness 5 mm and 2.5 mm	Reduced mAs	Standard dose CT KUB
Moore et al. [25]	America	2015	201	18+ (43.6)	105:96	3.4	64 detector row 2.5 mm slice thickness	Automated tube current modulation + tailored kVp for LD CT scans	Standard dose CT KUB

CTIVU, CT intravenous urography; ESWL, extracorporeal shock wave lithotripsy; LD, low dose; CT KUB, non-contrasted computed tomography scan of the kidney, ureter, and bladder.

endoscopic procedure or collection following spontaneous passage [28, 29, 31]. The final study used a combination of standard dose CT and physical stone demonstration [33].

Diagnostic Value of LD CT

Four studies investigated LD CT KUB [25–28]. They used mean effective radiation doses between 2.1 and 4.5 mSv. The sensitivity reported by these studies ranged from 90 to 98%. The specificity ranged from 88 to 100% (Fig. 2). The pooled sensitivity was 91.9% (CI: 87.8–95%) and the pooled specificity was 97.2% (CI: 94–99%) The corresponding ROC curve shown in Figure 3 assesses the accuracy of LD CT KUB for urinary tract stone detection.

Diagnostic Value of ULD CT

Eight studies investigated ULD CT KUB [8, 16, 29–34]. With each scan reviewer considered separately, this resulted in 12 data sets. Mean effective radiation doses used ranged from 0.48 to 1.9 mSv. The sensitivity ranged from 72 to 99%. Specificity ranged from 86 to 100% (Fig. 4). The pooled sensitivity was 95.2% (CI: 93.7–96.4%) and the pooled specificity was 96.9% (CI: 95.5–98%). The corresponding ROC curve shown in Figure 5 assessed the accuracy of ULD CT KUB for urinary tract stone detection.

Diagnostic Accuracy

The diagnostic accuracy for LD CT was 94.3% and for ULD CT was 95.5%.

Methodological Quality of the Included Studies

The quality of the reported studies was high overall (Fig. 6, 7). Consecutive patient selection was used across all the studies. Exclusions were not documented in 1 paper [29] and, as such, selection bias could not be accurately assessed in this case. No missing data were identified. Authors of studies were contacted, and their data were clarified where it was unclear to the reviewers [16]. No other sources of bias were identified.

Conclusions

Summary of Main Results

Reduced radiation dose CT KUB protocols are an effective imaging technique to accurately identify urolithiasis. The diagnostic accuracy for LD CT was 94.3% and for ULD CT was 95.5%. Sensitivity and specificity were consistently high in the LD CT group (90–98 and 88–100%). In the ULD CT group, high specificity and sensitivity

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Table 2. Baseline characteristics for ULD CT studies (mean radiation 0.48–1.9 mSv)

Study (ref.)	Country	Year	Number of patients	Age, range (mean)	Gender (M:F)	mSv	CT specifications	Dose reduction methods	Reference standard
Hamm et al. [29]	Germany	2002	109	20–84 (49)	76:33	1.12	4 detector row scanner, 5 mm slice thickness	Reduced kVp and reduced mA	Retrograde pyelography
Tack et al. [33]	Belgium	2003	106	15–84 (45)	53:53	1.5	4 detector row scanner, 3 mm slice thickness	Reduced mAs	Stone retrieval, standard dose CT, CTIVU
Kim et al. [30]	South Korea	2005	121	19–86 (44)	79:42	1.77	4 detector row scanner, 5 mm slice thickness	Reduced mAs	Standard dose CT KUB
Kluner et al. [31]	Germany	2006	142	18–83 (47)	74:68	0.60	16 detector row scanner, 1 mm and 5 mm slice thickness	Reduced mAs	Stone retrieval, clinical and imaging follow-up
Poletti et al. [32]	Switzerland	2007	125	19–80 (45)	87:38	1.75	4 detector row scanner, 5 mm slice thickness	Reduced mAs	Standard dose CT KUB
Mulkens et al. [16]	Belgium	2007	300	22–90 (51.4)	188:112	6	6 and 16 detector row scanners, 2 mm slice thickness	4D tube current modulation + reduced kVp in one subset	Endoscopic surgery
McLaughlin et al. [35]	America	2014	33	16–74 (45.2)	17:16	0.48	64 detector row, 0.625 mm slice thickness	Reduced kVp and fixed low mAs plus iterative reconstruction	Standard dose CT KUB
Fontarensky et al. [34]	France	2015	118	18–81 (42.9)	71:47	1.40	64 detector row Iterative reconstruction, 0.625 mm slice thickness	kVp tailored to BMI, mA modulation in subset, IR versus model based IR	Standard dose CT KUB

CTIVU, CT intravenous urography; ULD, ultra-low dose; CT KUB, non-contrasted computed tomography scan of the kidney, ureter, and bladder.

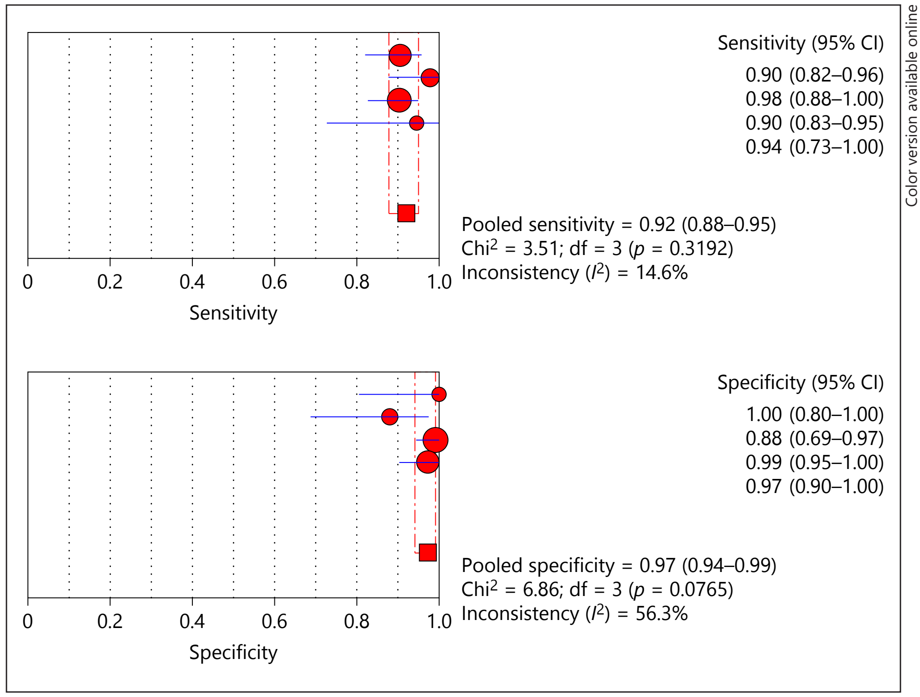

Fig. 2. Forest plots of sensitivity and specificity for low dose CT.

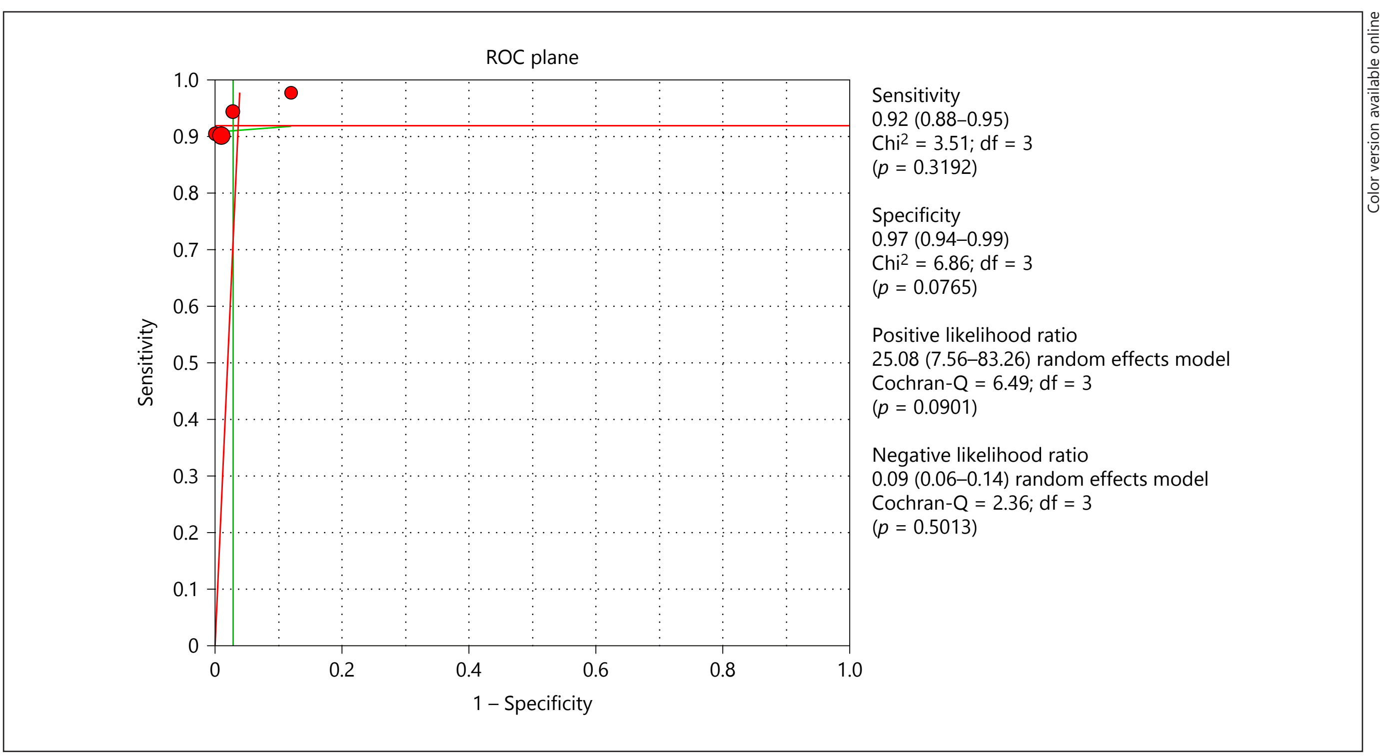

Fig. 3. Summary receiver operating characteristic curves plot of low dose CT.

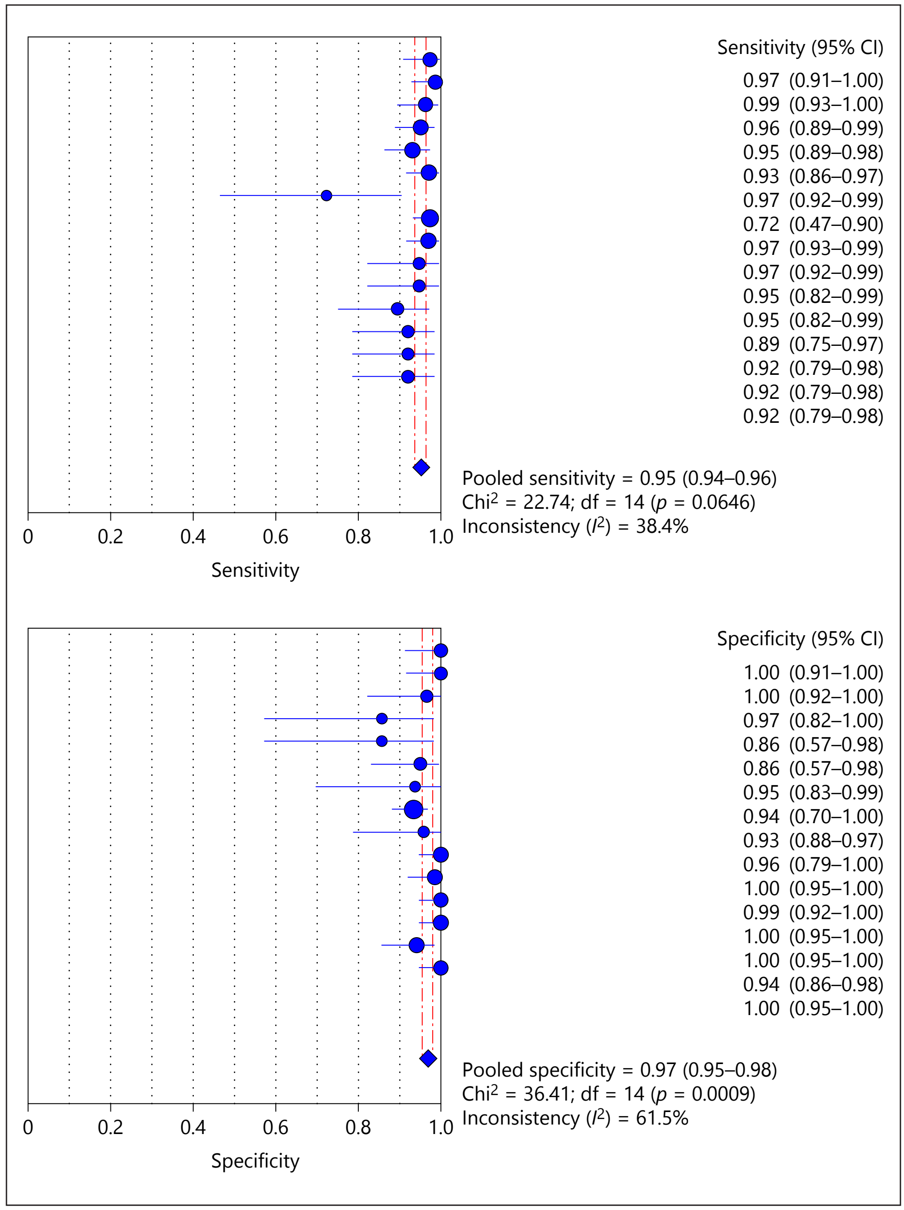

Fig. 4. Forest plot of sensitivity and specificity of ultra-low dose CT.

were maintained in the majority of papers (72–99 and 86–100%). These results are in keeping with initial feasibility studies [35]. Other recently published studies assessing the efficacy of LD CT KUB have reported data in keeping with these results [13, 14]. However, to our knowledge, we are the first group to report the diagnostic accuracy for LD and ULD dose CT KUB separately.

The lowest reported sensitivity value (72%) was reported by McLaughlin et al. [8] for ULD CT KUB. However, the researchers used a dosage of 0.48 mSv. This was the lowest reported across the studies in this review and is less than the radiation dose of a standard X-ray KUB. In spite of this, when their results were adjusted to include only stones greater than 3 mm, the sensitivity rose to 87%. Sensitivity of X-ray KUB for urolithiasis has been reported at as low as 40–60% [36]. The demonstration of this large discrepancy in sensitivity between 2 imaging modalities of the same radiation dose could provide justification for the use of ULD CT as the follow-up imaging modality of choice, therefore making X-ray KUB obsolete in this area.

It has been estimated that for every 10 mSv of radiation, the risk of developing a fatal cancer is 0.05% [37]. It has been suggested in the literature that sequential radiation exposures have a cumulative effect resulting in the

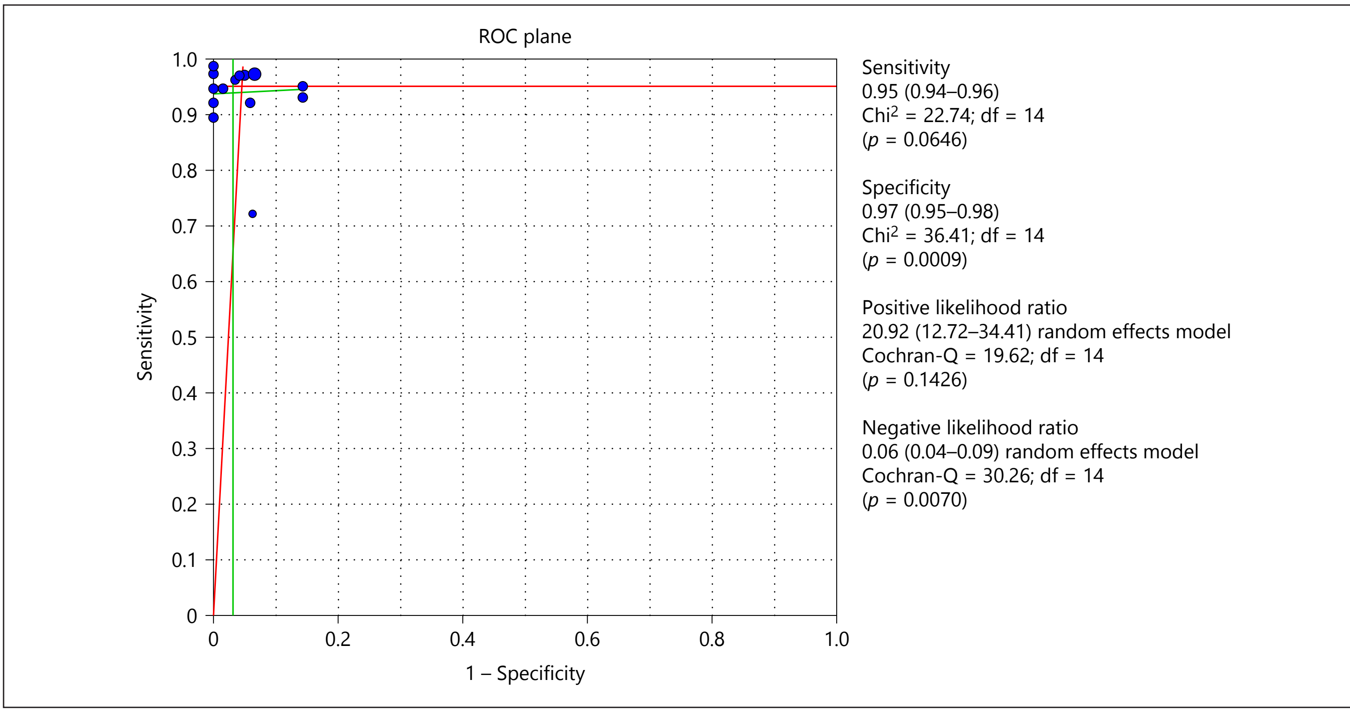

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Fig. 5. Summary receiver operating characteristic curves plot of 3 ultra-low dose CT.

same carcinogenic impact as single large doses [38]. Therefore, patients with recurrent renal colic are a group at particular risk. One study showed that over 10% of patients with recurrent renal colic were undergoing more than or equal to 1 CT per year with 1 patient in their analysis having 18 CTs over the 6-year follow-up period [39]. Renal colic often affects a relatively young patient group and it has been shown that the relative risk of radiation-related cancers is higher in younger patients [40]. This provides greater incentive to move toward LD protocols. The introduction of ULD CT in this group will significantly reduce lifetime radiation exposure and the associated risks.

One of the benefits in using CT KUB in acute flank pain is the added ability to identify diagnoses other than urinary tract stones. Many of the papers included in this review assessed the ability of reduced dose CT KUB to pick up alternative diagnoses as a secondary outcome. One paper demonstrated examples of significant alternative diagnoses such as acute appendicitis, which were missed on ULD CT. As such, there may still be a rationale for standard dose CT in patients where there is significant uncertainty about the underlying diagnosis. Nonetheless, this review demonstrated a high accuracy rate for cases of suspected stones for both CT modalities. Further research to assess the diagnostic accuracy of LD CT for alternative diagnoses would be required before LD protocols can be used in this way.

Strengths of This Study

This paper presents a comprehensive review of the existing literature based on Cochrane and STARD guidelines. This review gives an overview of the diagnostic accuracy of LD and ULD CT scans separately, showing high diagnostic yields. We were able to group a large number of studies to obtain an overall representative pooled analysis. In cases where the data have not previously been reported as clear TP, TN, FP and FN numbers, or have been reported on a stone-by-stone basis, efforts were made to contact publishing authors to gain access to as much data relevant to our research question as possible [16]. The sub-analysis of ULD scans separately from LD is particularly valuable as with advancing technology ULD scanning is becoming increasingly popular and feasible in clinical practice.

Limitations

In this review, we have grouped papers into LD and ULD CT groups on the basis of dosage in mSv. However, in each group, there was marked variation in the radiological protocol used across the studies which cover a decade and a half of publications and 4 generations of CT scanner hardware. The more recent studies employing more contemporary equipment have used as their reference CT scans performed with technologies that the initial papers would have considered state-of-the-art for LD. There is also methodological variation in the determination of dose as differing conversion factors used in several of the studies predating the most recent ICRP recommendations of 2008 in which the abdominal conversion factor remained the same, (0.015), but that for the pelvis decreased from 0.015 to 0.013, due to lower weighting factors for gonads and bladder. One study stratified patients into low and high BMI groups, using a greater current in the high BMI group. Another study stratified patients into 3 groups based upon BMI, mainly to determine appropriate kVp, which is in itself a major contributor to overall dose. Further research into specific patient groups for example obese patients may be of value.

It is clear that reduced dose protocols are effective. However, the different dose reduction strategies used in these studies mean that this review cannot make recommendations for a specific CT protocol. This is in part because of the different dose reduction strategies used and IR methodologies available. However, it is also because, with the advancement of technology in this area, many of the scanners used in the earlier papers are now technologically obsolete and techniques such as automated tube current modulation have become conventional day-to-day practice.

Implications for Practice

LD CT KUB maintains high sensitivity and specificity for the detection of urinary tract stones despite significant reductions in radiation. On the basis of this review, we believe in absolutely minimizing radiation dose in CT KUB protocols for the diagnosis of renal stones, acute renal colic, and the follow-up of such patients where required. Notwithstanding the limitations mentioned within this review, the basic principles of ALARA should always be adhered to and simple measures (such as minimizing the extent of coverage of CT KUB scans) that can significantly reduce exposure must be used ensure minimum radiation dose. Ongoing departmental audit of CT KUB radiation doses and factors influencing such is to be encouraged.

The exact methodology for LD CT KUB in any department will of course depend upon the equipment available. Where there is a choice of CT scanner, one which minimizes the radiation dose is to be preferred. This has the potential to reduce patient radiation exposure without compromising diagnostic accuracy. With modern CT systems and state-of-the-art IR solutions, ULD CT doses can be comparable with that of plain X-ray KUB. ULD CT

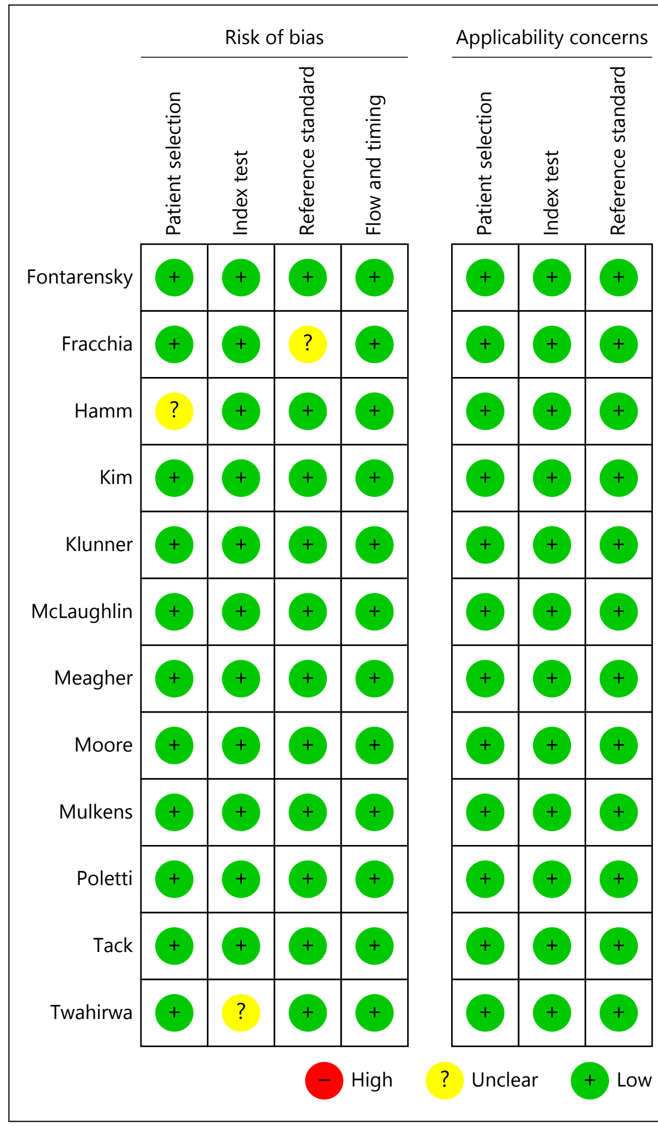

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Fig. 6. Risk of bias and applicability concerns graph: review authors' judgments about each domain presented as percentages across included studies.

may be of particular use in the follow-up of patients with known urinary tract stones to monitor the progress of stones of clinically relevant size as it has been shown that sensitivity improves with increased stone size [8]. This provides a potential solution to help the reduce radiation exposure associated with young patients who are recurrent stone formers. A cost analysis between standard, LD, and ULD scans will also greatly benefit decision process in requesting these scans. In the future, advancing MRI techniques may make zero radiation dose cross-sectional imaging for renal stone disease a clinical reality [41].

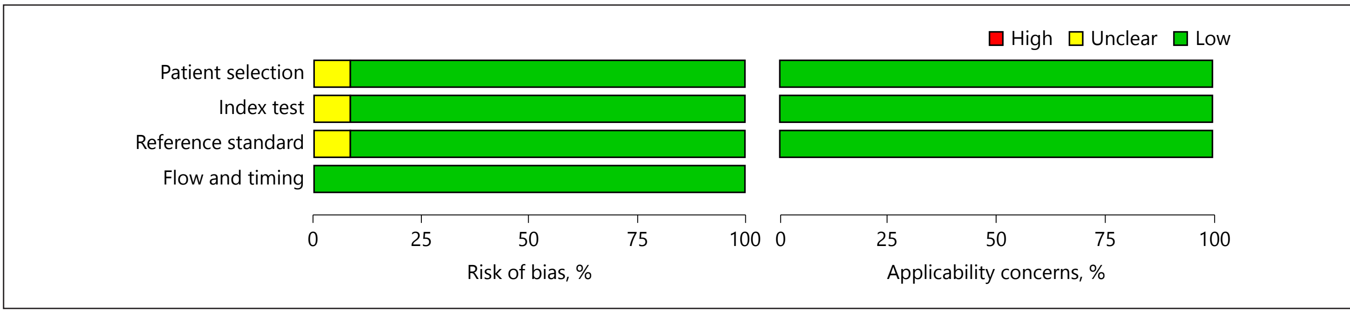

Fig. 7. Risk of bias and applicability concerns summary: review authors' judgments about each domain for each included study.

Implications for Future Research

With rapidly developing imaging technology, research should focus on ULD CT KUB with the aim to optimize the balance between low radiation exposure and high diagnostic accuracy. Further studies directly comparing the efficacy of different methods of dose reduction may help in achieving a consensus in this area. To allow meaningful conclusions to be made, we call for all future publications to give clear detail on the methodology of dose reduction, including technical factors (kVp, mAs, modulation methods, and IR methods) as well as stratifying by patient body habits. We also call for consistent reporting of radiation doses. When quoting doses in mSv the conversion factor used should be stated. We additionally encourage reporting of DLP and CTDIvol. Zero radiation dose techniques with MRI should also be explored, especially for the young and for follow-up examinations in known stone formers.

Take Home Messages

LD and ULD CT KUB scans provide effective methods of identifying and evaluating urinary tract stones. High diagnostic accuracy, sensitivity, and specificity are maintained despite significant radiation dose reduction compared to standard dose CT. This provides an opportunity to reduce lifetime radiation dose in patients with urinary tract stones and is of particular benefit in young patients with recurrent stones disease. Therefore, we strongly recommend that all patients with stone disease be considered for LD or ULD CT scans as opposed to standard dose CT scans.

Disclosure Statement

There are no conflicts of interest relevant to the preparation of this paper.

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