UNIVERSITÉ TOULOUSE III – PAUL SABATIER
FACULTÉS DE MÉDECINE

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THÈSE

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par

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PRETS POUR UN UTI-RADS ? ETAT DE L'ART : REVUE SYSTEMATIQUE DE LA LITTERATURE ET META-ANALYSE

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Up for UTi-RADS ? State of the art : a Systematic Review and Meta-Analysis

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ABSTRACT

Purpose

Frequently, upper urinary tract tumours are imprecisely diagnosed. Recent data have shown a benefit to adding systemic treatments to advanced local stage tumour (≥T2). In recent years, MRI has provided useful information to evaluate the local T stage of urinary bladder tumours, which may be used for the upper urinary tract.

Objective

The aim of the current study is to review the literature on the diagnostic and staging capability of MRI for upper urinary tract tumours. Additionally, the methods of performing MRI on the upper urinary tract were evaluated.

Methods

This systematic review was conducted according to the PRISMA using MEDLINE and EMBASE. All original articles published between January 2000 and May 2022 investigating MRI diagnosis and staging performances of MRI for patients with suspected upper urinary tract tumour were included in this research. We excluded meta-analyses, reviews, letters, meeting abstracts of unpublished trials, case reports, studies with no more than 20 cases and articles not written in English. Study quality assessment was performed by QUADAS-2 and MINORS tools. The performances were pooled separately using a random-effects model, we used bivariate model to compare imaging modalities.

Results

Overall, 14 studies were included consisting of 969 patients and 563 with upper urinary tract tumours. A wide heterogeneity of sequences was observed using the following techniques: standard acquisition (T1 weighted + T2 weighted), magnetic resonance urography (MRU) with dynamic contrast-enhanced imaging, functional imaging technique with diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC). While standard acquisition showed insufficient diagnosis performances, MRU and DWI presented strong diagnostic scores for pooled sensitivity (88.8% and 94%), specificity (88.1% and 85.2%) and accuracy of diagnosis (83% and 89.2%) respectively. DWI and ADC seemed to be informative for staging and prognostic evaluation. Based on this analysis, this study suggests that future studies on upper urinary tract MRI include T1W, T2W, MRU, DWI with high b-value (>800), and ADC analysis in the imaging protocol.

Conclusion

Medical imagery shows strong potential to positively enhance upper urinary tract tumours diagnosis and staging. With greater diagnostic power comes opportunities for improved patient treatment. Despite heterogeneous data and limited evidence, findings of this study suggest that further large multicentric studies should be conducted in order to better evaluate MRI diagnostic performances of upper urinary tract, with a predefined standard acquisition compared to the pathology report of radical nephroureterectomy or long-term follow-up by medical imaging.

INTRODUCTION

Urothelial carcinomas are the sixth most common tumour in developed countries [1]. Among them, bladder and urethra tumours account for 90%-95%, while upper urinary tract (pyelocaliceal cavities and ureter) tumours (UUTT) account for 5-10% of all urothelial carcinomas [1]. At diagnosis, the disease of approximately two third of patients is already invasive [2,3]. The prognosis for UUTT is reliable for non-infiltrating lesions (<pT2), but diminishes when UUTT invade the muscle wall [2,4].

Management of UUTT changes according to the tumour progression risk, ranging from endoscopic treatment with renal conservation to nephroureterectomy. Given the poor prognosis of invasive tumours, adjuvant platinum-based chemotherapy is recommanded [5–7]. Recent data even suggests the possibility of offering this chemotherapy as neoadjuvant treatment, often as patients are not cisplatin eligible due to the renal function impairment after a nephroureterectomy [8]. On one hand, preoperatively assessment of the tumour stage which is a crucial information to offer appropriate systemic treatment, remains difficult [9]. Currently, computerised tomography urography (CTU) is the reference imaging method, but requires contrast media injection and creatinine clearance above 30mL/min [10]. CTU has high diagnostic performances in detecting UUTT (sensitivity 92%; specificity 95%) [11]. However, diagnostic performances decrease for flat lesions or those smaller than 5 mm. On the other hand, CTU cannot differentiate a muscle-infiltrating (≥ T2) lesion from a non-infiltrating lesion (<T2). Additionally, the reliability of endoscopic upper tract biopsy in tumour stage evaluation is low, often underestimating invasion grade [12,13]. Importantly, performing a biopsy exposes the patient to higher risk of morbidity and mortality risks as compared to CTU, like a higher frequency of bladder recurrence and the risks related to general anaesthesia [14].

Recent data reported that MRI provides useful information for evaluating the local T stage of urinary bladder cancer, particularly in differentiating T1 stage or lower tumours from others [15–17]. The development of functional non-contrast imaging sequences, such as diffusion weighted imaging (DWI) showing in vivo water molecular diffusion, and apparent diffusion coefficient (ADC) which quantifies the extent of water molecule diffusion calculated using various DWI set with different b values, provides information about tissues biophysical properties such as cell organization and density, microstructure, and microcirculation [18,19]. These imaging sequences are used to differentiate benign and malignant lesions. Malignant lesions show high cellularity and intact cell membrane phenotype where restricted water motion is observed in a reduced extracellular space [18].

Up to now, the role of magnetic resonance imaging (MRI) in the diagnosis of UUTT is limited as an alternative to CTU in patients who present a CTU contraindication such as allergies or contraindications for radiation or iodinated contrast media [6,7]. However, given the added value of MRI in bladder cancer, our hypothesis was MRI can offer a useful preoperative diagnostic and staging tool of UUTT. Preoperative imaging technique that could differentiate T1 stages or lower tumours from others would represent a major advance in patients diagnosis, treatment and follow-up. The aim of the current study was to review the existing literature on MRI performances for the diagnostic and staging of UUTT. Additionally, the methods and sequences of performing MRI on the upper urinary tract were evaluated.

MATERIALS AND METHODS

Literature search strategy and study selection

The study protocol was registered in the PROSPERO database (study number CRD42022319265). A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist was followed for the study methodology (**Supplementary Table 1**) [20]. In order to review the entire literature published between January 2000 and May 2022, a systematic search of the major reference databases - MEDLINE (PubMed) and EMBASE (Elsevier) - was undertaken in May 2022. Key search terms included *ureter/upper urinary tract/renal pelvis, tumour/neoplasm/carcinoma/disease* and *magnetic resonance imaging/diffusion weighted imaging/apparent diffusion coefficient*. Details of search terms used for each database is reported on **Supplementary Table 2**.

Covidence software was used for literature management (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org.). After duplicate removal, two investigators (CM and LB) working in duplicate independently assessed all studies after conduction the primary search, according to their title and abstract with guidance from the predefined selection criteria. The same authors then made the final selection on the basis of the full-text versions of the studies and the predefined inclusion and exclusion criteria. They independently screened records for inclusion, blinded to each other's decisions. Discordances were discussed with a third reviewer (MR) and resolved by consensus.

Inclusion and Exclusion criteria

We included studies that analysed adult patient with suspected upper urinary tract tumours (Population) who underwent MRI for diagnosis, staging and/or prognosis evaluation (Intervention). Only prospective or retrospective human adult studies published in English between January 2000 and May 2022 were included. Pathological report after radical nephroureterectomy was considered as the reference standard for result comparison. However, studies using CTU, biopsy and ureteroscopy associated to active follow-up were also included (Comparison). We collected all variables that objectively assessed MRI reliability for diagnosis, staging and prognosis, and MRI modalities (Outcomes). Meta-analyses, reviews, letters, meeting abstracts of unpublished trials, case reports, studies with no more than 20 cases and articles not written in English were excluded from the study.

Data extraction

Relevant data for each selected article in a standardized form (**Supplementary table 3**) were extracted including: 1) general data of the article (title, authors, year of publication, journal), 2) study design characteristics (prospective or retrospective, unicentric or multicentric, consecutive vs non-consecutive enrolment, duration of patient recruitment, reference standard), 3) population characteristics (total number, carcinoma and no carcinoma number, tumour stage, number of patient with renal failure), 4) radiologist and pathologist characteristics (number of reader, experience, information on patient available for the interpretation of the exam), 5) MRI characteristics (magnet field strength, scanner model and manufacturer, coil, type of MRI sequences used and their corresponding technical parameters), 6) patient preparation (diuretic, empty or full bladder, conduct in case of haematuria) and 7) imaging performances (accuracy, sensitivity, specificity, inter reader agreement, false negative and false positive explanation).

Methodological Quality: Risk of Bias and Quality of Evidence

The risk of bias for all included studies were assessed by two investigators independently (CM and LB). We evaluated the methodological quality applied to four "risk of bias" domains and three "concerns regarding applicability" domains according to the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool [21], to which each item was

given a response of “yes”, “no” or “unclear”. The answer of “yes” means that the risk of bias of the study is low, while “no” and “unclear” meant that the risk of bias can be judged as high. We also used the Methodological Index for Non-Randomized Studies (MINORS) grading score for clinical studies [22]. MINORS score is a validated tool which uses eight graded questions for non-comparative studies. We judged each domain as presenting low, high, or unclear risk of bias by using a numeric score: each item can be scored as 0 (not reported), 1 (reported but inadequate) and 2 (reported and adequate). Ideal global score varies from 16 for non-comparative studies and 24 for comparative ones.

Statistical analysis

The performances of radiologic imaging were pooled separately using a random-effects model. Studies without extractable data were excluded from the meta-regression analysis. We used a bivariate model to summary estimates of sensitivity and specificity with corresponding 95% CI and tested for differences in sensitivity, or specificity, or both, between the different imaging modalities. Analyses were conducted using Microsoft Excel (v2019, Microsoft, USA, 2019) and open-source R software (version 3.6.2 ; R Foundation for Statistical Computing, Vienna, Austria) [23]. A p-value less than 0.05 was considered indicative of statistical significance ($\alpha = 0.05$). The graphs were realized using GraphPad Prism version 8.0.0 for Mac, GraphPad Software, San Diego, California USA, www.graphpad.com.

RESULTS

Identification and selection of studies

The PRISMA flowchart is presented in **Figure 1**. The 3262 studies used were imported for screening and 270 duplicates were removed. After title and abstract examination, 2961 studies were judged irrelevant. A further 31 studies were fully reviewed and 14 were finally included (17 excluded).

Studies characteristics

Amongst the 14 single-centre studies, 43% (n=6) were prospective whilst 57% (n=8) were retrospective (**Table 1**), with the most recent study published in 2018. All studied reports comprised a total of 969 patients of which 563 (58.1%) had an upper urinary tract tumour; and each study included between 35 to 163 patients with 20 to 100% presenting UUTT. Amongst included studies, 12 (86%) evaluated MRI diagnosis performances, and 4 (28%) evaluated staging and aggressiveness. Three studies (21%) compared MRI and CTU and one evaluated the ability of MRI to differentiate central renal cell carcinoma from renal pelvic urothelial carcinoma.

Studies included patients either with confirmed UUTT or with high suspicion of an UUTT (gross haematuria or upper urinary tract lesion on CTU). The reference standard followed pathology analysis (nephroureterectomy specimen or biopsy), or, if considered inappropriate, ureteropyelogram with 12 or 18 months follow up.

Studies evaluating the performances of MRI staging performances have compared T3 or higher tumours with T2 or lower tumours, but none have evaluated the ability to identify T2 or higher tumours.

12 (86%) studies had a double reading by two independent radiologists. Radiologist had between 3 and 30 years of training in renal MRI. Number and experience of pathologist that reviewed pathological pieces was not reported.

Technical MRI characteristics

MRI was performed using 1.5T system for 79% (n=11) studies et 3.0T system for the other studies. General electric healthcare, Siemens or Philips systems scanner were used with phased array coil, four or eight channel body coil. 93% (n=13) studies did T1W and T2W sequences, the other study performed T2W only. 50% (n=7) realized MRU sequences, 64% (n=9) performed DWI acquisition with different b-value (400, 500, 800, 1000, and 1500) and 14% (n=2) studies realized DCE and MRU sequences.

Sequences performances

MRI sequences used in the included studies were diverse. Baseline sequences such as T2 weighted (T2W) and T1 weighted (T1W) are systematically performed. MRU involve the use of contrast media agent with late phasis dynamic contrast-enhanced imaging diffusion weighted imaging (DCE). MRU is being questioned or could be improve by adding functional imaging DWI and ADC.

Firstly, we will present and analyse each sequence performances, secondly we will compare sequences performances.

Baseline sequences T1W and T2W

Diagnosis

4 studies evaluated performances of T1W and T2W (without MRU or DWI) [24–27] (**Table 2**) . Akita et al. (2011) [24] and Yoshida et al. 2017 [25] evaluated the diagnosis and staging performances exclusively in patients with UUTT. Wu et al. (2014) [26] and Yoshida et al. (2010) [27] evaluated in population with respectively 48% and 64 % patients with UUTT.

Pooled diagnosis performances showed 80.4% [95%IC 73.7-87.6%] sensitivity, 77.4% [95% IC 59.9-1.00%] specificity and 72.2% [95%IC 65.6-79.5%] accuracy (**Figure 2**).

The sensitivities of the different articles are heterogeneous, ranging from 63 to 87%, but the specificities are even more heterogeneous, ranging from 60 to 100% with very wide confidence intervals (**Table 2**).

Staging

The staging performance were evaluated by for Akita et al. (2011) [24] and Yoshida et al. (2017) [25]. The ≥T3b and ≤T3a tumours discrimination (60% to 76% sensitivity and 74 to 96% specificity) seems to be better than ≥T3 or versus ≤T2 (54% to 73% sensitivity and 64 to 84% specificity) but results are heterogeneous and not statistically significant (**Table 2**) [24,25]. Pooled statistics can't be performed due to non-extractable data.

Magnetic resonance imaging urography (MRU)

MRU is based on an association of T2W static-fluid acquisition and a late excretory imaging performed using gadolinium-enhanced T1W sequences (DCE) [28]. MRU is used as an interesting alternative of CTU to determine upper tract dilatation and exact location of obstruction in case of suspected obstructive uropathy [29].

Diagnosis

Diagnosis performance of MRU was studied in 7 studies [24,26,27,30–32] (**Table 2**). Pooled diagnosis performances showed 88.8% [95%IC 83.4-94.6%] sensitivity, 88.1% [95% IC 83.7-92.8%] specificity and 83.0% [95%IC 79.6-86.6%] accuracy (**Figure 2**).

Studies [30,31] showed that interpretation could be influenced by the quality of acquisition, a suboptimal distention and a poor opacification of the collecting system or ureters.

Staging

Staging performances varied between the two studies [24,25]. Sensitivity varied between 83-88% sensitivity and 78-100% specificity for ≥T3b and ≤T3a tumours discrimination and 65 to 78 % and specificity between 75 to 82% for ≥T3 and ≤T2 tumours discrimination.

Diffusion weighted MRI (DWI)

DWI is a functional imaging technique based on the molecular diffusion, it does not involve the use of a contrast media agent; the image contrast depends on the mobility of the water molecules in the tissue [19]. Some studies reported the DWI diagnostic performance for preoperative T categorization [24,27].

Diagnosis

A total of 6 studies evaluated tumour detection performance [24–27,33,34].

Pooled diagnosis performances showed 94.0% [95%IC 91.9-96.1%] sensitivity and 85.2% [95%IC 79.1-91.9%] specificity and 89.2% [95%IC 86.5-91.9%] accuracy (**Figure 2**). Pooled sensitivity were really high with a short confidence interval with data of 5 studies [24,25,34,35] (**Figure 2**). Interobserver agreement κ were excellent from 0,801 to 0,934 depending on the studies. Pooled specificity had a more dispersed distribution but b value seems to change specificity [34]. DWI acquisition was performed with a *b* value ranging from 400 to 1500 but DWI acquisition could impact the performance. Wu et al. (2013) [34] evaluated the performance of DWI with b values of 500 or 1500. High *b* values reduced increased specificity but did not change the sensitivity. Wu et al. (2013) [34] suggested that if a higher *b* value signal

is used, the intensity of non-malignant tissues decreases faster than those of malignant tissues, thus improving the ability to differentiate them.

Staging

Staging performances were interesting with 81-88% sensitivity and 96-100% specificity for ≥T3b and ≤T3a tumours discrimination [24,25]. The performances for ≥T3 and ≤T2 tumours discrimination were lower with 58-80% sensitivity and 77-93% specificity [24,25].

Apparent diffusion coefficient (ADC)

Apparent diffusion coefficient quantifies the extent of the water molecule diffusion calculated using various DWI with different b values (via changing gradient amplitudes) [36].

Six studies [25,35,37–40] suggested that ADC could be a prognostic marker. Statistically, the mean ADC value of the malignant lesions was significantly lower than both normal renal parenchyma and benign lesions [24,37]. Uchida et al. [38] demonstrated that lesions with a lower ADC value have a higher risk of developing metastasis. Yoshida et al. (2014) [40] demonstrated a significant inverse correlations of ADC with the histological grade and Ki-67 labelling index. Shebel et al. [35] defined the most significant cut off value of $1.5x10^3$ mm2/s to find the highest sensitivity and specificity of 79% and 82%, respectively for discriminating inflammatory lesions from urothelial tumours .

Performances comparisons

Pooled performances comparisons were not possible due to studies heterogeneity and the lack of consistent comparator between studies. Numerous studies compared different MRI sequences performances with each other.

MRI Diagnosis

Standard acquisition was performed in only 5 studies [24,25,27,34,35], no study performed this acquisition alone, it was always to compare with MRU and or DWI. Diagnosis performance were lower for standard acquisition in all studies, it was statistically significant in 3 studies [27,34,35].

Akita et al. (2011) [24] and Yoshida et al. (2017) [25] evaluated the diagnosis performance of standard acquisition against standard acquisition with MRU or standard acquisition with DWI in patient with confirmed UUTT. The tumour detection was not statistically different between acquisition. In patient populations including patients with suspected UUTT, Yoshida et al. (2010) [27] showed that DWI sensitivity and accuracy were significantly greater than those of standard acquisition, the specificity were higher, however without statistical significance. Likewise, Shebel et al. [35] found that DWI sensitivity, specificity, positive and negative predictive values and total accuracy in lesions detection were significantly higher ($p < 0.01$) than standard acquisition (T1W + T2W).

The diagnosis ability of DWI and MRU were not markedly different [27] but Wu et al. (2014) [26] showed an increase in sensitivity tumour diagnosis by adding DWI to MRU.

MRI Staging

Akita et al. (2011) [24] and Yoshida et al. (2017) [25] evaluated the performances to discriminate T3 or higher tumours from T2 or lower tumours and ≤T3a vs ≥ T3b with differences sequences. There were no significant difference between sequences, except from the accuracy to discriminate ≤T3a vs ≥ T3b tumours that was significantly better for standard acquisition with DWI than for standard acquisition alone ($p = 0.016$) [24].

Interestingly, less-experienced radiologist reader can increase their diagnosis performances by using additional sequences. For example, T2W plus DWI improved the accuracy and AUC results whilst MRU use improved the specificity, accuracy and AUC for

discriminating ≥T3b vs ≤T3a tumours [25]. Interobserver agreement regarding the T categorization was excellent for standard acquisition with DWI (κ=1) and MRU (κ=0,85) while it was good (κ=0,69) for standard acquisition alone [24].

Comparison with CTU

CT urography (CTU) is the reference imaging method for the diagnostic workup of UUTC in patients with creatinine clearance > 30 ml/min [10]. Currently, a total of 4 studies compared CTU with MRI with these setting [26,30,31,33] which results are heterogeneous.
Wu et al. (2014) [26] found that CTU had significantly greater sensitivity and accuracy than both MRU and MRU with DWI for the diagnosis. Martingano et al. [31] showed that CTU performances were statistically better than MRU for one radiologist but not for the second. Akita et al. (2018) [33] showed non-significant decreased sensitivity of DWI than CTU. In contrast, they showed that the specificity of DWI was higher than that of CTU (91% against 78% with p=0,065) [33]. In patients with suspicious CTU, DWI would be useful for identifying both mass-forming and wall-thickening lesions [33]. Adding DWI improved accuracy from 36% to 79% for wall-thickening lesions [33]. In patients with urinary obstruction and non-excreting kidney showed a statistically significant difference, with better overall image quality for MRU (p<0.01) [31].

Where MRI fails ?

False positive and negative diagnoses using MRI were collected for each study (**Table 3**). Whatever the sequence, MRI failed to detect carcinoma *in situ*. Due to section thickness and the intersection gap, small lesions were missed, with a cut-off range of 3 to 5mm [25,33,37].
Non-specific inflammation has always been considered as a suspicious lesion [27,33,34]. ADC acquisition could additionally differentiate inflammation from a malignant lesion [35]. Movement artifacts represent an important MRI interpretation challenge [31]. It can mimicked wall thickening. In these studies, CTU failed too: it didn't diagnose carcinoma in situ, misinterpret inflammation, benign urinary tract wall thickening, fibrosis, endometriosis and amyloidosis [33].

Performing an upper urinary tract MRI: conditions applied in selected studies

There is no current international consensus on optimal conditions for performing upper urinary tract MRI. Thereby, authors proposed different conditions for the selected studies.
Haematuria changes signal changes due to blood presence in urinary tract with increasing signal on DWI with a low ADC value. It is preferable to postpone the examination 2 weeks after an episode of gross haematuria [37].
MRI accuracy to detect upper urinary tract tumours tended to be lower in patients with ureteral stent or a nephrostomy tube [32], it cause urinary tract wall thickening that could mimic a urinary tumour [30,32]. It is not recommended to evaluate patients with a ureteral stent or nephrostomy tube by MRI alone.
Ureters and collecting systems distention seems to improve imaging analysis [31]. This is why 6 studies injected furosemide if no urinary dilatation was observed on the first sequence [30–32,37]. The dosage varies between but it could be recommended to inject furosemide if no urinary dilatation was observed. Thus, to avoid discomfort resulting from bladder overdistention at the end of the examination, patients were asked to void their bladder before the MRI examination was performed.
Some studies [25,31] supressed gastrointestinal peristalsis. This aimed to control motion artifact from gastrointestinal exercise with hyoscine-N-butylbromide administration. However, no evidence-based rationale supports this point.

Ureteroscopy in the previous days of imaging examination caused peri-urethral infiltration, it is preferable to postpone the examination [33,37].

Methodological Quality: Risk of Bias Assessment

Risk of bias assessment was presented **Figure 3**. Only two studies were considered to be at low risk of bias for all domains. A high risk of bias was deemed in 29% (n=4) of the studies due to lack of control cases ; they selected with patients with upper urinary tract tumour only. Additionally, 21% (n=3) of the studies informed radiologists of the presence of at least one upper urinary tract lesion on each examination, which introduced a bias. In 64% (n=9) of included studies, there was a high risk of bias for flow and timing due to unclear intervals between index test and reference standard and different reference standards between patients.

DISCUSSION

The diagnosis and follow-up of upper urinary tract tumours must be improved in order to be more accurate and less invasive. Differentiating T1 or lower stage tumours from T2 and higher stage tumours represents a new challenge for the management of our UUTT patients. Knowing that MRI is successful tool to diagnose bladder tumours [16], there is an exciting prospect that MRI could increase the accuracy of the diagnosis and the staging of the UUTT without general anaesthesia or radiation.

This work is the first systematic review including all currently available studies performed to evaluate the diagnostic performance of upper urinary tract MRI, three key concepts can be highlighted. Firstly, available literature data is scarce and no studies have been published for 4 years. Secondly, available studies included different populations and had heterogeneous design such as different MRI protocol yielding highly variable results. Thirdly, none of them evaluated the ability of MRI to differentiate between < T2 vs ≥T2 stage tumours, a crucial criterion for neoadjuvant systemic treatment indication in UUTT. To finish, contrary to the reference imaging (CTU), MRI can be used to assess prognosis and tissue structure.

Currently, CTU is the most frequently used imaging modality for upper urinary tract tumours diagnosis. It is a less expensive exam than MRI with high diagnosis performances [11]. However, it is an irradiating exam that requires a renal function above 30mL/min. MRI avoids radiation exposure and the use of contrast media injection. Furthermore, we have shown that MRI with functional non-contrast imaging sequences provides information beyond anatomical structure, with tissular structure and prognosis.

Among the three MRI protocols identified (T1W + T2W alone, with MRU or DWI), it seems clear that standard acquisition with T1W and T2W is insufficient and MRU and DWI performed better. Studies showed a statistically significant difference between standard acquisition and MRU or DWI [27,34,35], but diagnosis ability of DWI and MRU were not markedly different in varying studies [24,25,27]. Studies suggested that DWI could improve specificity [33,34].

It is interesting to note that despite the fact that DWI sequences are not anatomical and are difficult to read, less-experienced reader can increased its performances diagnosis by adding DWI sequences [25] and radiologist confidence [26].

Although there is no strong level of evidence, studies suggest that DWI was better for staging [24,25].

More interestingly, ADC quantitative data were associated with prognosis and histological features in several studies [24,25,35,37–39]. Lower ADC values were associated with malignancy and poor prognosis in these studies but the cut off ADC value to differentiate malignant from benign lesions or high risk and low risk tumours differed. A cut-off ADC is not universally applicable because the ADC depends on the MRI systems and imaging conditions used [41].

Functional magnetic resonance imaging, such as DWI and ADC, alone or combined with MRU represent interesting perspectives for upper urinary tract evaluation, with diagnosis, staging, and prognosis evaluation possibilities.

Based on this analysis, it seems essential that future studies on upper urinary tract MRI include T1W, T2W, MRU, DWI with high b-value (>800) and ADC analysis in imaging protocol. All of these sequences should be performed with a strong consensus in the conference from the French Society of Genitourinary Imaging [42].

According to the various studies in this review, upper urinary tract MRI should not be performed during an episode of gross haematuria or in the days following ureteroscopy, or with ureteral stent or nephrostomy tube. Preparation of patient proposed in the consensus conference from the French Society of Genitourinary Imaging [42] were confirmed in our study; distension

of both the collecting systems and the ureter is necessary for image interpretation. In case of no urinary obstruction, furosemide has to be injected and to avoid patient discomfort we can ask to void their bladder before the exam.

There are some limitations in this study. First, the small sample size of studies which influences the results accuracy and make it difficult to extract reliable performance parameters. The population differ with variability in clinical presentation of patients, in selection of patient from included studies and limits analysis. MRI sequences are heterogeneous so it is difficult to compare results. Finally, the major limitation of this review is the lack of high-level evidence evaluating MRI in the diagnosis of upper urinary tract tumour such as the heterogeneity of data, the lack of prospective studies and standardization of imaging.

This review summarises the current data on MRI of the upper urinary tract. Although the ideal imaging protocol needs to be clearly defined, upper tract MRI offers a real hope for the diagnosis and treatment of upper urinary tract tumours. MRI is a non-invasive exam that would allow more accurate assessment of the tumour stage. It could be used to diagnose and optimise treatment of UUTT but also to monitor the recurrence of the disease in our patients. This review will serve as a basis for future prospective studies.

CONCLUSION

The utility of MRI in the management of bladder tumours has grown and is becoming increasingly relevant, while the means of assessing and diagnosing upper urinary tract tumours remain imprecise and invasive. This review has shown the lack of evidence data about MRI usefulness and its diagnosis performance for upper urinary tract tumour. However, these results and the adding of DWI sequences are encouraging and suggest interesting perspective for upper urinary tract tumour diagnosis, treatment and management. This review should encourage new prospective studies and facilitate their design having reviewed the current data available and identified the modalities of performing MRI for upper urinary tract assessment.

A large multicentre study evaluating the diagnostic performance of upper urinary tract MRI with a predefined standard acquisition (including T1W, T2W, DWI and MRU acquisition) compared to the pathology report of radical nephroureterectomy or long-term follow-up by medical imaging will be proposed.

Vu et permis d'imprimer

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LEGEND

Figure 1 : Flowchart of study's selection

Figure 2 : Forest plots of studies included in the meta-analysis show individual and pooled estimates for diagnostic sensitivity (A.), specificity (B.), accuracy (C.), with 95% confidence interval.

Abbreviation : CI : confidence interval ; CTU : computed tomography urography ; DWI : diffusion weighted imaging ; MRU : magnetic resonance urography ; T2W : T2 weighted ; T1W : T1 weighted.

Figure 3 : Methodological Quality : Risk of Bias Assessment QUADAS-2 (A.) and MINORS (B.)

Table 1 : Characteristics of the studies included

Abbreviation : ADC : apparent diffusion coefficient ; CT : computed tomography ; CTU : computed tomography urography ; DWI diffusion weighted imaging ; MRI : Magnetic resonance imaging ; MRU : magnetic resonance urography ; nb : number ; T2W : T2 weighted ; T1W : T1 weighted ; T : Tumour ; yr : year.

Table 2 : Diagnosis performances of MRI for upper urinary tract tumour.

Abbreviation: ADC : apparent diffusion coefficient ; AUC : area under the curve ; CTU : computed tomography urography ; DWI diffusion weighted imaging ; MRI : Magnetic resonance imaging ; MRU : magnetic resonance urography ; nb : number ; T2W : T2 weighted ; T1W : T1 weighted ; T : Tumour.

Table 3 : Where MRI fails ?

Abbreviation: CTU : computed tomography urography ; DWI : diffusion weighted imaging ; MRI : Magnetic resonance imaging ; MRU : magnetic resonance urography ; T2W : T2 weighted ; T1W : T1 weighted.

Supplementary Table 1 : PRISMA 2020 Checklist and abstract checklist

Supplementary Table 2 : Details of search terms

Supplementary Table 3 : Standardized form used for data extraction

FIGURES

Figure 1 : Flowchart of study's selection
*Articles studied different sequences, this is why there are more sequences than articles

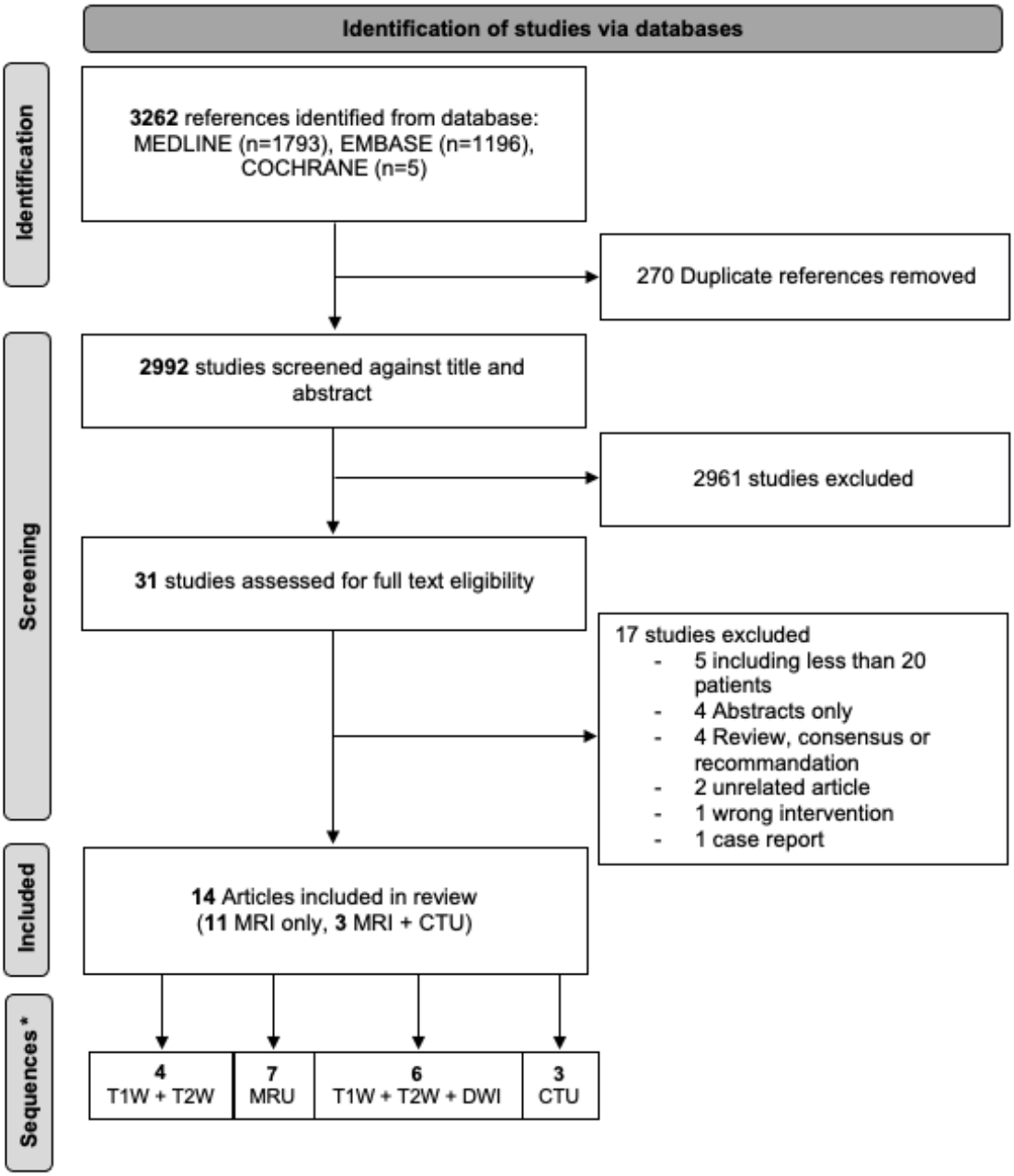
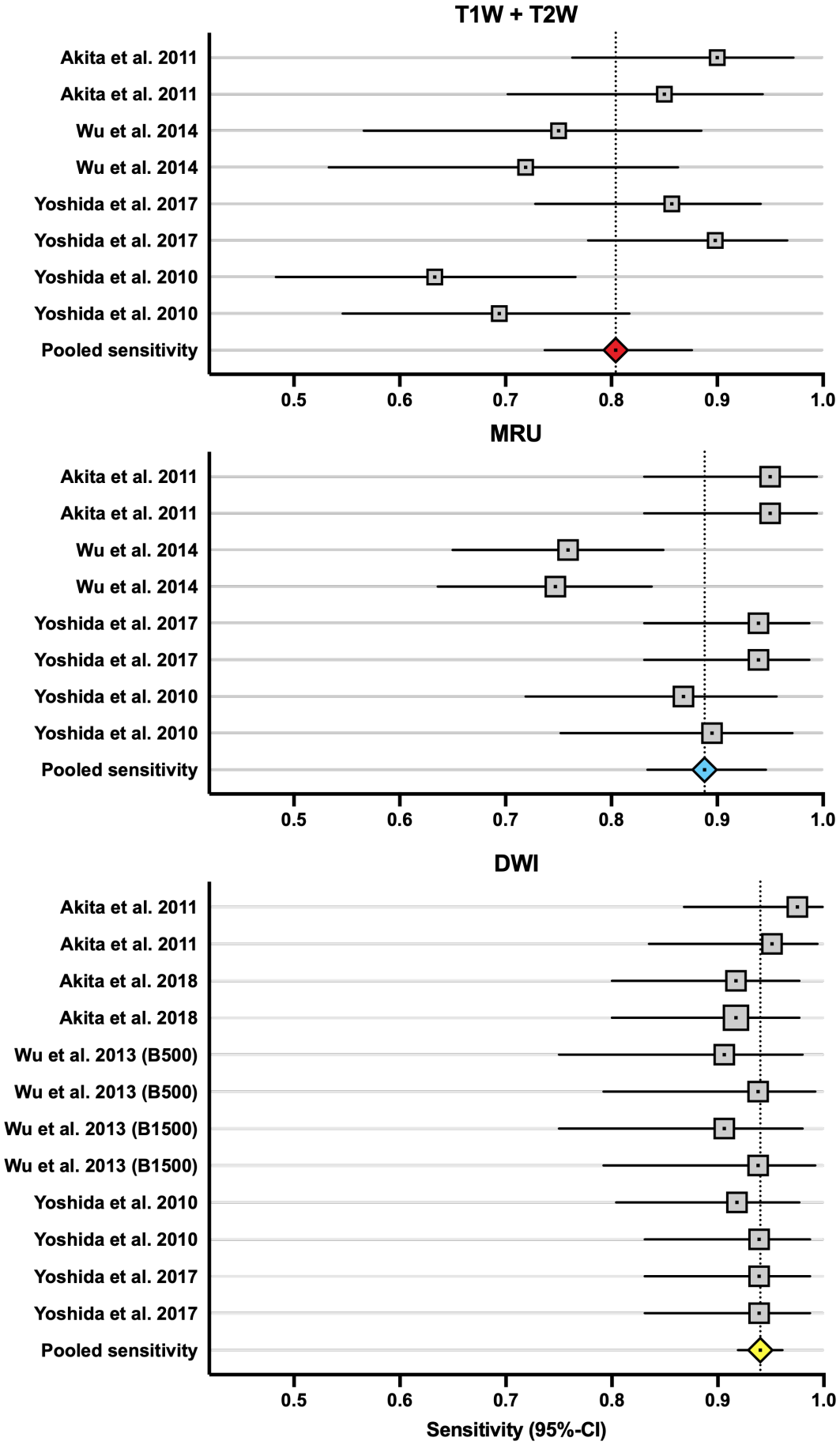
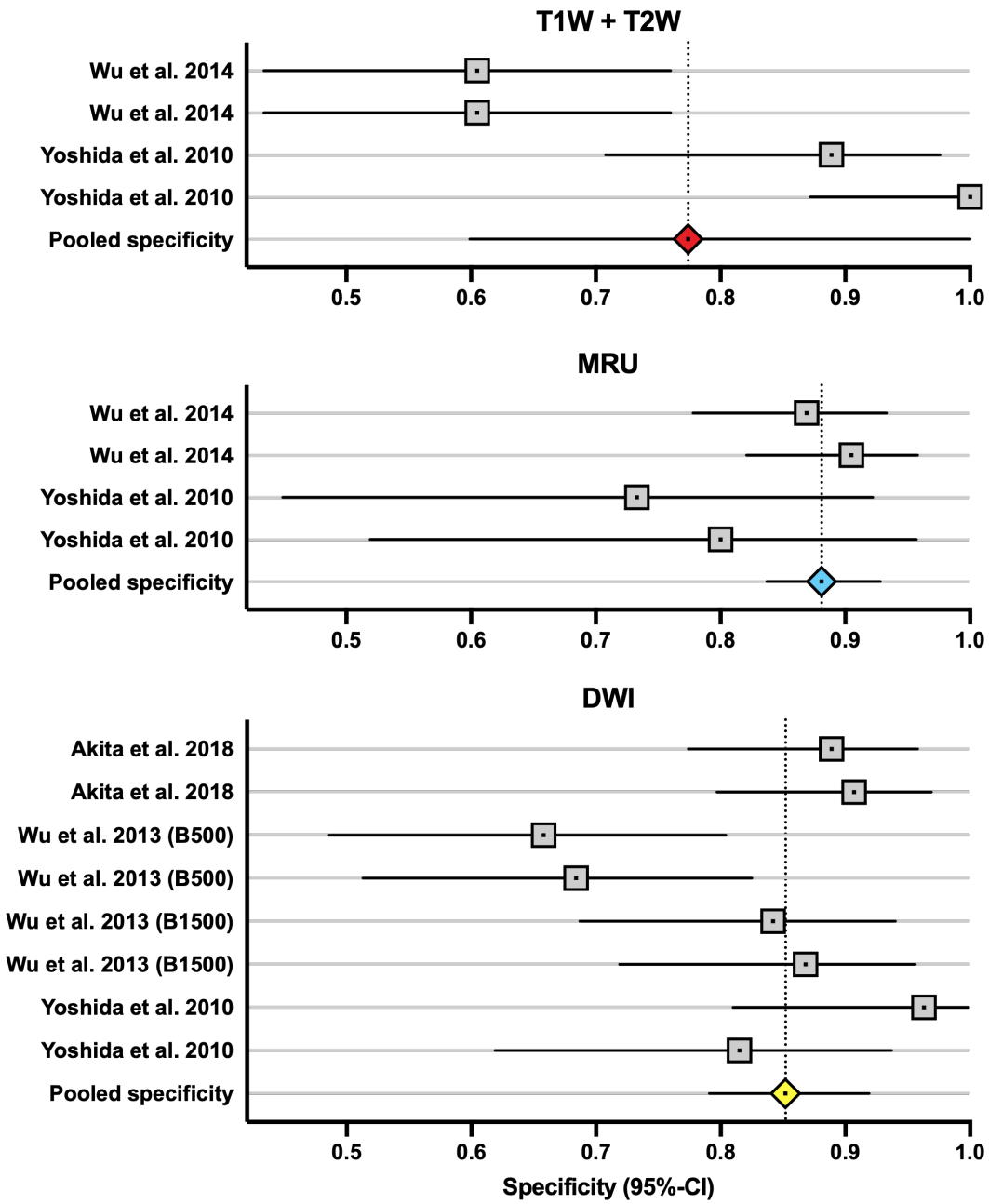


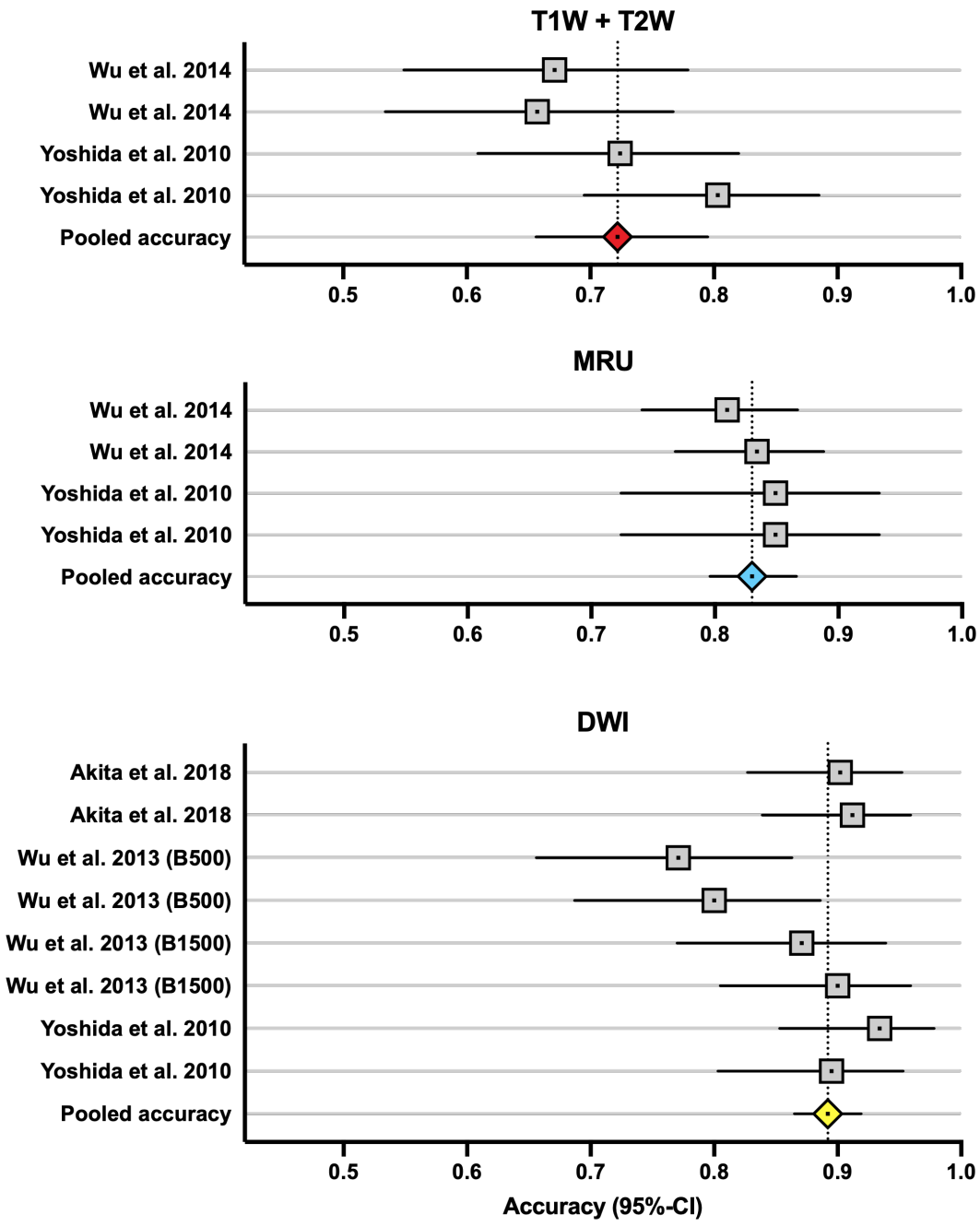
Figure 2 : Forest plots of studies included in the meta-analysis show individual and pooled estimates for diagnostic sensitivity (A.), specificity (B.), accuracy (C.), with 95% confidence interval (CI).



A.


T1W + T2W
Wu et al. 2014
Wu et al. 2014
Yoshida et al. 2010
Yoshida et al. 2010
Pooled specificity
0.5
0.6
0.7
0.8
0.9
1.0
MRU
Wu et al. 2014
Wu et al. 2014
Yoshida et al. 2010
Yoshida et al. 2010
Pooled specificity
0.5
0.6
0.7
0.8
0.9
1.0
DWI
Akita et al. 2018
Akita et al. 2018
Wu et al. 2013 (B500)
Wu et al. 2013 (B500)
Wu et al. 2013 (B1500)
Wu et al. 2013 (B1500)
Yoshida et al. 2010
Yoshida et al. 2010
Pooled specificity
0.5
0.6
0.7
0.8
0.9
1.0
Specificity (95%-CI)

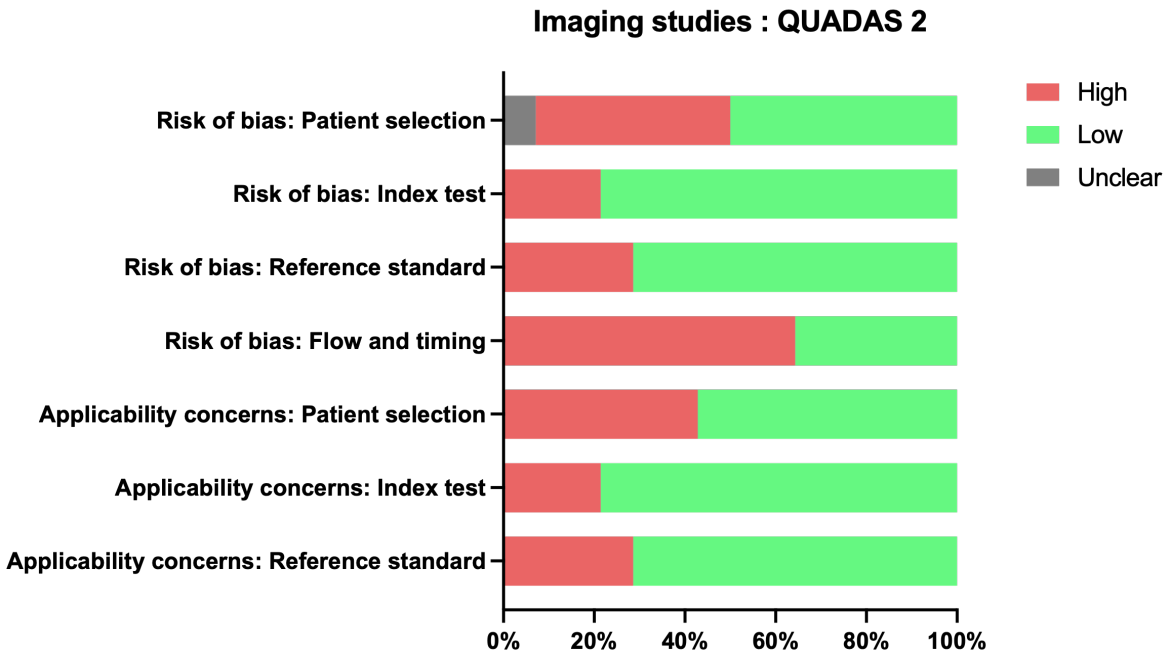
B.


T1W + T2W
Wu et al. 2014
Wu et al. 2014
Yoshida et al. 2010
Yoshida et al. 2010
Pooled accuracy
0.5
0.6
0.7
0.8
0.9
1.0
MRU
Wu et al. 2014
Wu et al. 2014
Yoshida et al. 2010
Yoshida et al. 2010
Pooled accuracy
0.5
0.6
0.7
0.8
0.9
1.0
DWI
Akita et al. 2018
Akita et al. 2018
Wu et al. 2013 (B500)
Wu et al. 2013 (B500)
Wu et al. 2013 (B1500)
Wu et al. 2013 (B1500)
Yoshida et al. 2010
Yoshida et al. 2010
Pooled accuracy
0.5
0.6
0.7
0.8
0.9
1.0
Accuracy (95%-CI)

C.

Figure 3 : Methodological Quality : Risk of Bias and Quality of Evidence.

A. Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS 2) tool.
B. Methodological Index for Non-Randomized Studies (MINOR) tool.



A.

B.

Table 1 : Characteristics of the studies included

Legend :

Abbreviation : ADC : apparent diffusion coefficient ; CT : computed tomography ; CTU : computed tomography urography ; DWI diffusion weighted imaging ; MRI : Magnetic resonance imaging ; MRU : magnetic resonance urography; nb: number ; imaging, T2W : T2 weighted ; T1W : T1 weighted ; T : Tumour ; yr : year.

Study	Objective	Prospective/ retrospective	Nb of patient with upper urinary tract tumour/ total nb of patient	Sequences	Nb of radiologist (experience)	Comparisons	Reference standard
Akita et al. 2011 Preoperative Tumor Categorization and Prediction of Histopathologic Grading of Urothelial Carcinoma in Renal Pelvis Using DWI	To evaluate the utility of DWI for preoperative T categorization and prediction of the histopathologic grade of renal pelvic cancer. (T3 or Higher Tumors From T2 or Lower Tumors/ T3b or Higher Tumors From T3a or Lower Tumors)	Retrospective	N= 40/40	T1W T2W MRU DWI(b1000)	2 (15yr, 11yr)	T1W+T2W vs MRU vs T1W+T2W+DWI	Nephroureterectomy pathology
Akita et al. 2018 Performance of DWI post-CT urography for the diagnosis of upper tract urothelial carcinoma: Comparison with selective urine cytology sampling	To evaluate the usefulness of adding DWI to CT urography for diagnosing upper tract urothelial carcinoma.	Retrospective	N=48/102	T1W T2W DWI(b1000) CTU	2 (30yr, 15yr)	T1W+T2W+DWI vs CTU	Nephroureterectomy or biopsy pathology, 2 years follow up imaging examination
Lee et al. 2010 Magnetic resonance urography versus retrograde pyelography/ ureteroscopy for the exclusion of upper urinary tract malignancy	To evaluate the diagnostic performance of magnetic resonance urography versus retrograde pyelography and/or ureteroscopy in the detection of upper urinary tract neoplasms.	Retrospective	N=19/35	T1W T2W MRU	1 (not reported)	MRU vs ureteroscopy-ureteropyelography	Biopsy, more than 1 year follow up imaging examination
Martingano et al. 2013 Magnetic resonance urography vs computed tomography urography in the evaluation of patients with haematuria	To evaluate by direct comparison the image quality of magnetic resonance urography and computed tomography urography and to assess the diagnostic confidence of the two techniques in detecting urothelial malignancy in patients with haematuria	Retrospective	N=19/35	T1W T2W MRU CTU	2 (not reported)	MRU vs CTU	Nephroureterectomy or biopsy pathology, follow up imaging examination
Roy et al. 2015 DWI in the Etiologic Diagnosis of Excretory Upper Urinary Tract Lesions : Can It Help in Differentiating Benign From Malignant Tumors ?	To evaluate the diagnostic performance of high-field DWI in distinguishing benign from malignant lesions of the upper urinary tract	Retrospective	N=66/98	T1W T2W DWI(b1000) ADC	2 (4yr , 8yr)	T1W+T2W+DWI Quantitative ADC	Nephroureterectomy or biopsy pathology, cytology, more than 1 year follow up imaging examination
Shebel et al. 2014 Characterization of upper urinary tract urothelial lesions in patients with gross hematuria using DWI : A prospective study	To evaluate the utility of DWI and ADC values in differentiation between malignant and non malignant lesions of the upper urinary tract in patients with gross hematuria.	Retrospective	N=23/51	T1W T2W DWI(b800) ADC	2 (≥10yr)	T1W+T2W vs T1W+T2W+DWI and ADC	Nephroureterectomy or biopsy pathology, cytology, 3 months clinical follow up
Takahashi et al. 2009 Gadolinium Enhanced Magnetic Resonance Urography for Upper Urinary Tract Malignancy	To evaluate the accuracy of gadolinium enhanced magnetic resonance urography to detect upper urinary tract tumors. Subgroup : surveillance/non surveillance/stent	Retrospective	N=28/91	T1W T2W MRU	2 (not reported)	MRU	Nephroureterectomy or biopsy pathology, 1 year follow up imaging examination

Uchida et al. 2014 Diffusion-weighted MRI as a potential imaging biomarker reflecting the metastatic potential of upper urinary tract cancer	To evaluate the role of DWI as an imaging biomarker for upper urinary tract cancer that has already metastasized or will metastasize soon.	Prospective	N=61/61	T1W T2W DWI(b400 or 800)	2 (7yr, 7yr)	ADC quantitative for metastatic potential	Nephroureterectomy or biopsy pathology, cytology, more than 1 year follow up imaging examination
Wehrli et al. 2013 Utility of MRI Features in Differentiation of Central Renal Cell Carcinoma and Renal Pelvic Urothelial Carcinoma	To evaluate the utility of various morphologic and quantitative MRI features in differentiating central renal cell carcinoma from renal pelvic urothelial carcinoma	retrospective	N=12/60	T1W T2W DWI(b400-800) ADC	2 (10yr, 10yr)	DWI with ADC and subjective imaging feature to differ renal cell carcinoma from urothelial carcinoma.	Pathologically proven renal urothelial carcinoma and renal cell carcinoma
Wu et al 2013 Imaging of upper urinary tract cancer: using conventional MRI and diffusion-weighted MRI with different b values	To evaluate the performance of using conventional MRI alone and in combination with DWI with different b values in diagnosis upper urinary tract cancer	Prospective	N=32/70	T1W T2W DWI (b500 and b1500)	2 (6yr, 6yr)	T1W+T2W vs T1W+T2W+DWI (b500) vs T1W+T2W+ DWI (b1500)	Nephroureterectomy or biopsy pathology, cytology, more than 18 months follow up imaging examination
Wu et al. 2014 Comparison of computed tomography urography, magnetic resonance urography and the combination of DWI in diagnosis of upper urinary tract cancer	To evaluate the performance of CT Urography, static fluid magnetic resonance urography and combination of CT urography MR urography and diffusion weighted imaging in the diagnosis of upper urinary tract cancer	Prospective	N=79/163	T1W T2W MRU CTU	2 (8yr, 8yr)	MRU vs T1W +T2W+DWI vs CTU vs CTU + DWI vs CTU+MRU+DWI	Nephroureterectomy or biopsy pathology, cytology, more than 18 months follow up imaging examination
Yoshida et al. 2010 Usefulness of DWI in Diagnosis of Upper Urinary Tract Cancer	To prospectively evaluate the diagnostic ability of DWI for detecting upper urinary tract cancer	Prospective	n=49/76	T1W T2W MRU DWI(b800)	2 (4yr, 4yr)	T1W+T2W vs MRU vs T1W+T2W+DWI	Nephroureterectomy or biopsy pathology, 1 year follow up imaging examination
Yoshida et al. 2014 ADC as a prognostic biomarker of upper urinary tract cancer : a preliminary report	To investigate the role of ADC as a biomarker reflecting the aggressiveness of upper urinary tract urothelial cell carcinoma.	Prospective	N=38/38	T1W T2W DWI (b400 or 800) ADC	Not reported	ADC quantitative	Nephroureterectomy pathology
Yoshida et al 2017 The value of adding DWI for tumor detection and preoperative staging in renal pelvic carcinoma for the reader's experience	To assess the value of adding DWI or gadolinium-enhanced fat-suppressed T1W to T2W imaging for preoperative T categorization in renal pelvic carcinoma by the reader's experience using surgical specimens as the reference standard.	Retrospective	N=49/49	T2W MRU DWI(b800)	2 (3yr, 13 yr)	T2W vs T2W+DCE vs T2W+DWI	Nephroureterectomy or biopsy pathology

Table 2 : Diagnosis performances of MRI for upper urinary tract tumour.

Legend :

Abbreviation : ADC : apparent diffusion coefficient ; AUC : area under the curve ; CTU : computed tomography urography ; DWI diffusion weighted imaging ; MRU : magnetic resonance urography ; nb : number ; T2W : T2 weighted ; T1W : T1 weighted ; T : Tumour.

Study	N= (nb cancer// percent cancer) Comparison	Sensitivity	Specificity	Accuracy	AUC	Inter observer agreement
T1W + T2W						
Akita et al. 2011	N=40 (40//100%) Tumour detection ≤ T2 vs ≥ T3 ≤ T3a vs ≥ T3b	 36-34/40 (88%) 14/26 (54%) 13/17 (76%)	 9/14 (64%) 17/23 (74%)	 23/40 (58%) 30/40 (75%)	 0,73 [0,55-0,92] 0,87 [0,72-1,00]	 0,69
Wu et al. 2014	N=70 (32//46%) Tumour detection	 23-24/32 (72-75%)	 23-23/38(61%)	 46-47/70 (66-67%)	 	 0,80
Yoshida et al. 2010	N=76 (49//64%) Tumour detection	 31-34/49 (63-69%)	 24-27/27 (89-100%)	 55-61/76 (72-80%)	 	 0,68
Yoshida et al. 2017	N=49 (49//100%) Tumour detection ≤ T2 vs ≥ T3 ≤ T3a vs ≥ T3b	 42-44/49 (86-90%) 69-73% 60-75%	 82-84% 95-96%	 73-78% 73-86%	 0,77-0,79 0,77-0,87	 0,429 0,431
MRU						
Akita et al. 2011	N=40 (40//100%) Tumour detection ≤ T2 vs ≥ T3 ≤ T3a vs ≥ T3b	 38-38/40 (95%) 17/26 (65%) 15/17 (88%)	 11/14 (79%) 18/23 (78%)	 28/40 (70%) 33/40 (83%)	 0,79 [0,65-0,93] 0,87 [0,80-1,00]	 1,0
Lee et al. 2010	N=113 (19//17%) Tumour detection	 12/19 (63%)	 86/94 (91%)	 98/113 (87%)	 	
Martingano et al. 2013	N=35 (29//83%) Tumour detection *regions	 83-86% (a lot of indeterminate segment)	 83-83%	 83-84%	 0,938-0,907	 0,71
Takahashi et al. 2009	N=91 (28//31%) Tumour detection *regions	 26-22/35 (74-62%)	 212-211/219 (97-96%)	 238-233/254 (94-92%)	 	 0,73
Wu et al. 2014	N=163 (79//48%) Tumour detection	 60-59/79 (76-75%)	 76-73/84 (90-87%)	 136-132/163 (83-81%)	 0,828-0,917	 0,874
Yoshida et al. 2010	N=53 (38//72%) Tumour detection	 33-34/38 (87-89%)	 12-11/15 (80-73%)	 45-45/53 (85-85%)	 	 0,72
Yoshida et al. 2017	N=49 (49//100%) Tumour detection ≤ T2 vs ≥ T3 ≤ T3a vs ≥ T3b	 46-46/49 (93%) 78-76% 83-86%	 82-75% 100-100%	 80-76% 92-94%	 0,755-0,755 0,864-0,950	 0,427 0,670
T1W + T2W + DWI						
Akita et al. 2011	N=40 (40//100%) Tumour detection ≤ T2 vs ≥ T3 ≤ T3a vs ≥ T3b	 39-39/40 (98%) 15/26 (58%) 15/17 (88%)	 13/14 (93%) 22/23 (96%)	 28/40 (70%) 37/40 (93%)	 0,79 [0,67-0,91] 0,96 [0,89-1,00]	 0,85
Akita et al. 2018	N=102 (48//47%) Tumour detection	 44-44/48 (96-96%)	 48-49/54 (89-91%)	 92-93/102 (90-91%)	 	
Wu et al. 2013	N=70 (32//46%) Tumour detection b500 Tumour detection b1500	 29-30/32 (91-94%) 29-30/32 (91-94%)	 25-26/38 (66-68%) 32-33/38 (84-87%)	 54-56/70 (77- 80%) 61-63/70 (87-90%)	 	 0,88 0,86
Yoshida et al. 2010	N=76 (49//64%) Tumour detection	 45-46/49 (92-94%)	 26-22/27 (96-81%)	 71-68/76 (93-89%)	 	 0,801
Yoshida et al. 2017	N=49 (49//100%) Tumour detection ≤ T2 vs ≥ T3 ≤ T3a vs ≥ T3b	 46-46/49 (93%) 74-80% 81-83%	 77-79% 93-100%	 76-80% 88-92%	 0,754-0,796 0,864-0,933	 0,755 0,712

CTU						
Akita et al. 2018	N=102 (48//47%) Tumour detection	46-47/48 (96-98%)	42-42/54 (78-78%)	88-89/102 (86-87%)		
Martingano et al. 2013	N=35 (29//83%) Tumour detection *regions	97-97% A LOT OF INDETERMINATE SEGMENT	91-87%	92-88%	0,994-0,977	0,43
Wu et al. 2014	N=163 (79//48%) Tumour detection	75-74/79 (95-94%)	75-74/84 (89-88%)	150-148/163 (92-91%)	0,919-0,912	0,947

Table 3 : Where MRI fails ?

Legend :

Abbreviation : CTU : computed tomography urography ; DWI diffusion weighted imaging ; MRI : Magnetic resonance imaging ; MRU : magnetic resonance urography ; T2W : T2 weighted ; T1W : T1 weighted.

Study	False negative	False positive
T1W + T2W		
Wu et al 2013 Imaging of upper urinary tract cancer: using conventional MRI and diffusion-weighted MRI with different b values		Non-specific inflammation Urothelial hyperplasia Ureteral papilloma
MRU		
Lee et al. 2010 Magnetic resonance urography versus retrograde pyelography/ureteroscopy for the exclusion of upper urinary tract malignancy		Ureteral stents in situ demonstrated ureteral wall enhancement, a small ureteral neoplasm could not be definitively excluded.
Martingano et al. 2013 Magnetic resonance urography vs computed tomography urography in the evaluation of patients with haematuria	Small lesion	Filling defects Movement artefacts mimicking wall thickening
Takahashi et al. 2009 Gadolinium Enhanced Magnetic Resonance Urography for Upper Urinary Tract Malignancy	Small renal pelvis lesion <4mm Carcinoma in situ	Ureteral stone causing ureteral wall thickening Inflammatory ureteral stricture
T1W + T2W + DWI		
Akita et al. 2018 Performance of DWI post-CT urography for the diagnosis of upper tract urothelial carcinoma: Comparison with selective urine cytology sampling	Ureter small papillary tumour <5mm Carcinoma in situ Renal pelvis small papillary tumour	Inflammation Benign urinary tract wall thickening High signal intensity in renal papilla on DWI
Roy et al. 2015 DWI in the Etiologic Diagnosis of Excretory Upper Urinary Tract Lesions : Can It Help in Differentiating Benign From Malignant Tumours ?	Carcinoma in situ Small lesion <3mm	
Wu et al 2013 Imaging of upper urinary tract cancer: using conventional MRI and diffusion-weighted MRI with different b values		Non-specific inflammation Urothelial hyperplasia Ureteral papilloma
Yoshida et al. 2010 Usefulness of DWI in Diagnosis of Upper Urinary Tract Cancer	Carcinoma in situ Papillary ureteral cancer in the vesicoureteral junction (3 mm) Renal pelvic cancer with congested renal parenchyma	Ureteral inflammation Ureteral stenosis
Yoshida et al 2017 The value of adding DWI for tumour detection and preoperative staging in renal pelvic carcinoma for the reader's experience	Small lesion Diffuse thin lesion	
CTU		
Akita et al. 2018 Performance of DWI post-CT urography for the diagnosis of upper tract urothelial carcinoma: Comparison with selective urine cytology sampling	Ureter small papillary tumour Carcinoma in situ	Inflammation Benign urinary tract wall thickening Fibrosis Endometriosis Amyloidosis
Martingano et al. 2013 Magnetic resonance urography vs computed tomography urography in the evaluation of patients with haematuria	Insufficient contrast medium excretion in obstructed patients	

Supplementary Table 1 : PRISMA 2020 Checklist and abstract checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	p1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	p2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	p3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	p3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	p4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	p4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	p4 + sup table 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	p4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	p4 + Fig 1
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	p4 + sup table 3
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	p4 + sup table 3
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	p5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	p5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	p5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	p5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	sup table 3

Section and Topic	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	p5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	p5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	p5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	p5
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	p5
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	p6 + fig 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	p6 + fig 1
Study characteristics	17	Cite each included study and present its characteristics.	p6 + Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	p10 + Fig 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	p10
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	p6-8 + Fig 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	p6-9
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	p6-8 + Fig 2
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	p10 + Fig 3
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Fig 2
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	p11
	23b	Discuss any limitations of the evidence included in the review.	p12
	23c	Discuss any limitations of the review processes used.	p12
	23d	Discuss implications of the results for practice, policy, and future research.	p12

Section and Topic	Item #	Checklist item	Location where item is reported
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	p4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	p4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not appropriate
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Not appropriate
Competing interests	26	Declare any competing interests of review authors.	p1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not appropriate

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

Supplementary Table 2 : Details of search terms

Search Strategy for MEDLINE (PubMed)	
Key words	((("ureter"[MeSH Terms] OR "ureteral diseases"[MeSH Terms] OR (("upper"[All Fields] OR "uppers"[All Fields]) AND ("urinary tract"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields]) OR "urinary tract"[All Fields])) OR (("upper"[All Fields] OR "uppers"[All Fields]) AND ("urinary tract"[MeSH Terms] OR ("urinary"[All Fields] AND "tract"[All Fields]) OR "urinary tract"[All Fields]) AND ("carcinoma, transitional cell"[MeSH Terms] OR ("carcinoma"[All Fields] AND "transitional"[All Fields] AND "cell"[All Fields]) OR "transitional cell carcinoma"[All Fields] OR ("urothelial"[All Fields] AND "carcinoma"[All Fields]) OR "urothelial carcinoma"[All Fields])) OR ("ureter"[MeSH Terms] OR "ureter"[All Fields] OR "ureters"[All Fields] OR "ureter s"[All Fields] OR "uretic"[All Fields]) OR ("kidney pelvis"[MeSH Terms] OR ("kidney"[All Fields] AND "pelvis"[All Fields]) OR "kidney pelvis"[All Fields] OR ("renal"[All Fields] AND "pelvis"[All Fields]) OR "renal pelvis"[All Fields]) OR ("carcinoma, transitional cell"[MeSH Terms] OR ("carcinoma"[All Fields] AND "transitional"[All Fields] AND "cell"[All Fields]) OR "transitional cell carcinoma"[All Fields] OR ("urothelial"[All Fields] AND "carcinoma"[All Fields]) OR "urothelial carcinoma"[All Fields])) AND ("diffusion magnetic resonance imaging"[MeSH Terms] OR "diffusion tensor imaging"[MeSH Terms] OR "magnetic resonance imaging"[MeSH Terms] OR ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields] OR "mri"[All Fields]) OR (("diffusable"[All Fields] OR "diffusant"[All Fields] OR "diffusants"[All Fields] OR "diffuse"[All Fields] OR "diffusely"[All Fields] OR "diffuses"[All Fields] OR "diffusibility"[All Fields] OR "diffusible"[All Fields] OR "diffusion"[MeSH Terms] OR "diffusion"[All Fields] OR "diffused"[All Fields] OR "diffusing"[All Fields] OR "diffusions"[All Fields] OR "diffusive"[All Fields] OR "diffusively"[All Fields] OR "diffusivities"[All Fields] OR "diffusivity"[All Fields]) AND ("weight s"[All Fields] OR "weighted"[All Fields] OR "weighting"[All Fields] OR "weightings"[All Fields] OR "weights and measures"[MeSH Terms] OR ("weights"[All Fields] AND "measures"[All Fields]) OR "weights and measures"[All Fields] OR "weight"[All Fields] OR "body weight"[MeSH Terms] OR ("body"[All Fields] AND "weight"[All Fields]) OR "body weight"[All Fields] OR "weights"[All Fields])) OR ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields]) OR ("diffusion magnetic resonance imaging"[MeSH Terms] OR ("diffusion"[All Fields] AND "magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "diffusion magnetic resonance imaging"[All Fields]) OR (("diffusable"[All Fields] OR "diffusant"[All Fields] OR "diffusants"[All Fields] OR "diffuse"[All Fields] OR "diffusely"[All Fields] OR "diffuses"[All Fields] OR "diffusibility"[All Fields] OR "diffusible"[All Fields] OR "diffusion"[MeSH Terms] OR "diffusion"[All Fields] OR "diffused"[All Fields] OR "diffusing"[All Fields] OR "diffusions"[All Fields] OR "diffusive"[All Fields] OR "diffusively"[All Fields] OR "diffusivities"[All Fields] OR "diffusivity"[All Fields]) AND ("magnet s"[All Fields] OR "magnetical"[All Fields] OR "magnetically"[All Fields] OR "magnetics"[MeSH Terms] OR "magnetics"[All Fields] OR "magnetic"[All Fields] OR "magnetisation"[All Fields] OR "magnetisations"[All Fields] OR "magnetised"[All Fields] OR "magnetism"[All Fields] OR "magnetisms"[All Fields] OR "magnetization"[All Fields] OR "magnetizations"[All Fields] OR "magnetize"[All Fields] OR "magnetized"[All Fields] OR "magnetizing"[All Fields] OR "magnets"[MeSH Terms] OR "magnets"[All Fields] OR "magnet"[All Fields]) AND ("image"[All Fields] OR

	"image s"[All Fields] OR "imaged"[All Fields] OR "imager"[All Fields] OR "imager s"[All Fields] OR "imagers"[All Fields] OR "images"[All Fields] OR "imaging"[All Fields] OR "imaging s"[All Fields] OR "imagings"[All Fields])) OR "dwi"[All Fields] OR ("arch dis child"[Journal] OR "acta dermatovenerol croat"[Journal] OR "adc"[All Fields]) OR ("apparent"[All Fields] AND ("diffusable"[All Fields] OR "diffusant"[All Fields] OR "diffusants"[All Fields] OR "diffuse"[All Fields] OR "diffusely"[All Fields] OR "diffuses"[All Fields] OR "diffusibility"[All Fields] OR "diffusible"[All Fields] OR "diffusion"[MeSH Terms] OR "diffusion"[All Fields] OR "diffused"[All Fields] OR "diffusing"[All Fields] OR "diffusions"[All Fields] OR "diffusive"[All Fields] OR "diffusively"[All Fields] OR "diffusivities"[All Fields] OR "diffusivity"[All Fields]) AND ("coefficiencies"[All Fields] OR "coefficiency"[All Fields] OR "coefficient"[All Fields] OR "coefficient s"[All Fields] OR "coefficients"[All Fields]))))
Publication period	(2000:2022[pdat]))
Search filters	AND Full text ((fft[Filter]); AND english[Filter])

Search Strategy for Embase	
Key words	('mri'/exp OR 'mri' OR 'magnetic resonance imaging' OR 'magnetic resonance urography' OR 'diffusion magnetic imaging' OR 'DWI' OR 'diffusion weighted imaging') AND ('upper urinary tract urothelial carcinoma'/exp OR 'upper urinary tract urothelial carcinoma' OR 'ureteral neoplasm' OR 'upper urinary tract' OR 'ureter disease' OR 'ureter' OR ‘renal pelvis)
Publication period	01-01-2000]/sd NOT [01-05-2022]/sd
Search filters	[english]/lim NOT ('nonhuman'/de OR 'case report'/de OR 'medical record review'/de OR 'meta analysis'/de OR 'systematic review'/de)

Search Strategy for The Cochrane Library (Cochrane Central Register of Controlled Trials)	
Key words	Upper urinary tract* in Title Abstract Keyword OR ureter* in Title Abstract Keyword OR renal pelvis* in Title Abstract Keyword AND magnetic resonance imaging* in Title Abstract Keyword OR apparent diffusion coefficient* in Title Abstract Keyword OR diffusion weighted imaging* in Title Abstract Keyword - (Word variations have been searched)
Publication period	01/01/2000 to 01/05/2022
Search filters	∅

Supplementary Table 3 : standardized form used for data extraction

General data of the article				Study design characteristics					Population characteristic									Radiologist and pathologist characteristics						MRI characteristic										Result					
												Tumour stage							Radiologist			Pathologist																		
Title	Authors	Year of publication	Journal	Prospective/retrospective	Unicentric/multicentric	Consecutive/non consecutive enrolment	Duration of patient recruitment	Reference standard	Total Number	Carcinoma number	No carcinoma number	Cis number	Ta number	T1 number	T2 number	T3 Number	T4 Number	Number of patient with renal failure	Number of radiologist	Experience of radiologist	Patient information for the	Number of pathologist	Experience of pathologist	Patient information for the	Magnet field strength	Scanner model	Manufecturer	Coil	T1W	T2W	CE	DWI	DCE	Set analysis	Accuracy	Sensitivity	Specificity	Inter reader agreement	False negative explanation	False positive explanation

GROUPEMENT INTERREGIONAL DE RECHERCHE CLINIQUE ET D'INNOVATION
GIRCI SOHO
SUD-OUEST OUTRE-MER HOSPITALIER

LETTRE D'INTENTION

DRCI : ❑ **CHU BORDEAUX** ❑ **INSTITUT BERGONIE** ❑ **CHU LIMOGES**
❑ **CHU MARTINIQUE** ❑ **CHU MONTPELLIER** ❑ **ICM**
❑ **CHU NIMES** ❑ **CHU POINTE-A-PITRE** ❑ **CHU POITIERS**
❑ **CENTRE C. REGAUD** ❑ **CHU LA REUNION** ☒**CHU TOULOUSE**

INFORMATIONS GENERALES

Titre du projet :
Essai prospectif étudiant l'intérêt de l'IRM dans le diagnostic des tumeurs de la voie excrétrice urinaire supérieure

Investigateur coordonnateur *(joindre CV)*

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Fonction : Chef de Clinique Assistant Spécialité : Urologie
Service : Urologie, Andrologie et transplantation rénale
Adresse électronique : manceau.c@chu-toulouse.fr
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Ville : Toulouse

(à cocher)

☑ Médecin ❑ Biologiste ❑ Paramédicaux
❑ Chirurgien-Dentiste ❑ Infirmière ❑ Sage-femme
❑ Autre

Etablissement-coordonnateur responsable du budget pour le Ministère de la santé

CHU de TOULOUSE

Domaine de Recherche

Diagnostic des tumeurs de la voie excrétrice urinaire supérieure, Imagerie par IRM.

Nombre prévisionnel de centres d'inclusion (NC)

5 : - CHU Toulouse Hôpital Rangueil
- Clinique Beausoleil, AESIO santé, Montpellier (Dr Grégoire Poinas)
- Hôpital Saint Louis APHP (Pr Alexandra Masson Lecomte)
- Clinique Pasteur Toulouse (Dr Alexandre Gryn)
- Clinique de la Croix du SUD Toulouse (Dr Pradère Benjamin)

PROJET DE RECHERCHE

Rationnel (contexte et hypothèses)

Les tumeurs urothéliales représentent la 6ième cause de cancer dans les pays développés. Elles sont présentes dans tout l'appareil urinaire (urètre, vessie, uretère et cavités pyelocalicielles). Les tumeurs de la voie excrétrice urinaire représentent 5 à 10% des carcinomes urothéliaux. 2/3 de ces patients présentent au diagnostic une tumeur invasive (≥ T2).
Actuellement le diagnostic des tumeurs de la voie excrétrice urinaire supérieure repose sur la tomodensitométrie avec injection de produit de contraste iodé néphrotoxique (uroTDM) et la réalisation de biopsies au cours d'une urétéroscopie sous anesthésie générale (1;2).
Les tumeurs invasives sont de mauvais pronostic et les patients atteints d'une tumeur infiltrante pourraient bénéficier d'une chimiothérapie néoadjuvante, avant la néphro-urétérectomie (susceptible d'altérer la fonction rénale) (3).
L'uroTDM ne permet pas de différencier une tumeur invasive d'une tumeur non invasive (4). Par ailleurs, les biopsies réalisées au bloc opératoire au cours d'une urétéroscopie sous anesthésie générale sont peu fiables pour évaluer le stade tumoral et sous estiment fréquemment la maladie. Le diagnostic des tumeurs infiltrantes se fait le plus souvent sur les pièces de néphro-urétérectomies, rendant impossible le traitement néoadjuvant.
Récemment des séquences IRM fonctionnelles (DWI, ADC) permettent de mettre en évidence les propriétés biophysiques des tissus telles que l'organisation cellulaire, la densité, la microcirculation et permettent ainsi de différencier les lésions bénignes et malignes et le niveau d'atteinte tissulaire. L'IRM est d'ailleurs devenu un réel outil dans le diagnostic des tumeurs vésicales et permet de différencier les lésions infiltrantes des non infiltrantes (5).

Le diagnostic des tumeurs urothéliales et l'évaluation du stade tumoral par IRM représenterait une avancée majeure et permettrait d'optimiser les prises en charge, en proposant notamment une chimiothérapie néoadjuvante aux patients présentant une maladie infiltrante. Par ailleurs cet examen pourrait être utilisé pour le suivi de ces maladies qui actuellement se fait par urétéroscopie et contrôle tomodensitométrique.

Originalité et caractère innovant

Contrairement aux examens actuels, le diagnostic par IRM est non invasif (pas d'anesthésie, pas de chirurgie), et ne nécessite pas d'injection de produit de contraste iodé (néphrotoxique). Par ailleurs il permettrait de mieux caractériser la tumeur (stade, grade, pronostic), ce qui est à ce jour inaccessible sans l'analyse anatomopathologique de la pièce opératoire.
Actuellement aucune étude prospective rigoureuse sur une large population n'a été réalisée.

Objet de la Recherche

Technologies de santé *(cocher & préciser) :*

❑ *médicaments :*
❑ *dispositifs médicaux*
☑ *actes : IRM de la voie excrétrice urinaire supérieure*
❑ *organisations du système de soins (incluant les services de santé)* [(2).]

(1) http : //htaglossary.net
(2) Conformément à l'instruction n° DGOS/PF4/2016/382 du 9 décembre 2016 relative aux Appels à Projets 2017 :
Les soins primaires englobent les notions de premier recours, d'accessibilité, de coordination, de continuité et de permanence des soins. Les soins primaires constituent la porte d'entrée dans le système qui fournit des soins de proximité, intégrés, continus, accessibles à toute la population, et qui coordonne et intègre des services nécessaires à d'autres niveaux de soins. S'ils sont le premier contact des patients avec le système de soins, les soins primaires sont également structurant pour la suite du parcours du patient au sein du système de santé.

Projet de recherche portant sur les « Soins premiers » [3]

❑ OUI ☑ NON

Mots Clés (5)

Cancer urothélial, tumeur de la voie excrétrice urinaire supérieure, IRM, diagnostic, non-invasif.

Objectif Principal

L'objectif de cette étude est d'évaluer à partir d'une séquence IRM prédéfinie les performances diagnostiques et d'évaluation du stade tumoral de l'IRM de la voie excrétrice urinaire supérieure.

(A cocher)

❑ *Description d'hypothèses*	❑ *Faisabilité*	❑ *Tolérance*
☑ *Efficacité*	❑ *Sécurité Efficience*	❑ *Impact budgétaire*
❑ *Organisation des soins*		

(A cocher)

❑ *Etiologie*	❑ *Thérapeutique (impact sur des critères de jugement cliniques "durs")* [5]
❑ *Causalité* [4]	
☑ *Diagnostic*	❑ *Thérapeutique (impact sur des critères de jugement intermédiaires)* [6]
☑ *Pronostic*	
❑ *Recherche sur les méthodes*	❑ *Observance*
❑ *Recherche qualitative*	❑ *Pratique courante*
❑ *Autre*	

Séquence IRM prédéfinie comprenant :
T1W, T2W, DCE (sans injection de produit de contraste, séquence au temps artériel, séquence au temps à l'équilibre, séquence tardive), DWI (b800, b1000, b1500, b2000).
3 radiologues (un junior et deux séniors) liront les images selon une grille de lecture pré définie.
L'utilité de chaque valeur de b sera évaluée.

Objectifs Secondaires

-Etude de l'apport des cytologies urinaires associées aux données de l'IRM pour le diagnostic des tumeurs de la voie excrétrice urinaire supérieure.
- Etude des valeurs de b les plus informatives pour le diagnostic et la stadification.

Critère d'évaluation principal (en lien avec l'objectif principal)

Sensibilité, spécificité, aire sous la courbe pour la détection d'une tumeur de la voie excrétrice urinaire supérieure.
Sensibilité, spécificité, aire sous la courbe pour l'identification d'une tumeur invasive vs non invasive de la voie excrétrice urinaire supérieure.

Critères d'évaluation secondaires (en lien avec les objectifs secondaires)

Performances diagnostiques de l'IRM associées aux résultats des cytologies urinaires.
Score d'utilité de chaque séquence ADC en fonction de la valeur du b.

(3) Etude visant à déterminer les causes d'une pathologie, le risque d'être exposé à un médicament, un polluant
(4) Exemple : réduction de la mortalité lors de la survenue d'infactus du myocarde
(5) Exemple : réduction du cholestérol sérique, amélioration sur une échelle de douleur

Population d'étude

(Principaux critères d'inclusion et de non inclusion)

Critères d'inclusion :

- Patient ayant plus de 18 ans, ayant une suspicion de tumeur de la voie excrétrice supérieure basée sur une hématurie macroscopique récidivante sans anomalie à la fibroscopie vésicale, ou la présence d'une lésion suspecte sur un uroTDM.

Critères de non inclusion :

- Insuffisance rénale ne permettant pas l'injection de produit de contraste iodée (DFG <30mL/min)
- Sujet sous protection juridique (tutelle ou curatelle)

Plan expérimental

❑ *Méta-analyse*
❑ *Etude contrôlée randomisée*
Si oui : ❑ Ouvert ❑ Simple Aveugle ❑ Double Aveugle
❑ *Revue systématique*
❑ *Etude pragmatique*
❑ *Etude quasi-expérimentale (cohortes non randomisées, …)*
☑ *Etude de cohorte prospective*
❑ *Etude cas-contrôle*
❑ *Etude transversale*
❑ *Etude de cohorte rétrospective*
❑ *Recherche dans les bases de données médico-administratives*
❑ *Modélisation*
❑ *Série de cas*
❑ *Autre*
❑ *Etude qualitative*

Essai clinique prospectif.
Les patients inclus auront une suspicion de tumeur de la voie excrétrice urinaire supérieure (basée sur une hématurie macroscopique récidivante (>1) sans anomalie à la fibroscopie vésicale, ou la présence d'une lésion suspecte sur un uroTDM).
Dans les 7 jours suivant leur inclusion, ils auront dans le cadre du bilan un UroTDM, et une IRM de la voie excrétrice supérieure et ils réaliseront des cytologies urinaires.

En cas de tumeur de la voie excrétrice urinaire supérieure la prise en charge sera discutée en réunion de concertation pluridisciplinaire d'oncourologie.

Les résultats de l'IRM seront comparés aux résultats anatomopathologiques (considérés comme le gold standard) ou en l'absence de lésions suspectes aux données d'imagerie (uroTDM) et de suivi à 12 mois.
Si une biopsie est réalisée, les données seront colligées, si une néphro-urétérectomie ou une urétérectomie segmentaire est réalisée les résultats anatomopathologiques de la pièce primeront sur les biopsies.
En cas de lésion bénigne ou en l'absence de lésion, un nouveau contrôle par uroTDM et IRM sera réalisé 12 mois après.

Durée de la participation de chaque patient
12 mois

Durée prévisionnelle de Recrutement (DUR)
24 mois

Nombre de patients / observations prévu(e)s à recruter (NP)

200 patients screenés, pour 150 patients inclus.
Le taux de patients présentant une tumeur maligne des voies excrétrices peut être estimé à 80%.
Le taux de patients présentant une tumeur maligne invasive des voies excrétrices peut être estimé à 120.

Participation d'un réseau de recherche

CCAFU (comité de cancérologie de l'association française d'urologie)

Participation de partenaires industriels
Non

Autres éléments garantissant la faisabilité du projet

L'uroIRM est un examen non invasif, actuellement recommandé en alternative à un uroTDM.

Les investigateurs ont déjà mené à bien des études prospectives, et sont par ailleurs impliqués dans plusieurs projets de recherche clinique.

Les centres d'urologie réalisent plusieurs néphro-urétérectomie par an, ce qui garantit une inclusion rapide des patients.

Bénéfices attendus pour le patient et/ou pour la santé publique

Si cette étude est concluante, cela permettrait une meilleure prise en charge des patients atteints d'une tumeur de la voie excrétrice urinaire supérieure. L'IRM représenterait un diagnostic fiable et non invasif. Il pourrait aussi être utilisé pour le suivi de ces patients.
Par ailleurs l'identification des maladies invasives en pré-opératoire permettrait de rendre accessible la chimiothérapie néoadjuvante à un plus grand nombre de patient, et améliorerait leur pronostic. Elle pourrait également permettre d'envisager un traitement conservateur avec plus de sécurité et épargner une nephroureterectomie.

D'un point de vu médico-économique le cout d'une IRM est largement inférieur à celui d'une prise en charge chirurgicale par urétéroscopie.

Cette étude devrait permettre une modification de la prise en charge des patients et des recommandations, et une amélioration majeure pour le diagnostic, le traitement et le pronostic des patients atteints d'une tumeur de la voie excrétrice urinaire supérieure.

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PRETS POUR UN UTI-RADS ? ETAT DE L'ART : REVUE SYSTEMATIQUE DE LA LITTERATURE ET META-ANALYSE

RESUME EN FRANÇAIS :

Les tumeurs des voies urinaires supérieures sont souvent diagnostiquées de manière imprécise. Des données récentes ont montré un bénéfice à ajouter des traitements systémiques pour des tumeurs de stade local avancé (≥T2). Ces dernières années, l'IRM a fourni des informations utiles pour évaluer le stade T local des tumeurs de la vessie, qui pourraient être utilisées pour les voies urinaires supérieures.

L'objectif de cette étude est de passer en revue la littérature sur les capacités de diagnostic et de stadification de l'IRM pour les tumeurs des voies urinaires supérieures. De plus, les acquisition et les modalités de réalisation de l'IRM sur les voies urinaires supérieures ont été évaluées.

Au total, 14 études ont été incluses, portant sur 969 patients dont 563 (58%) étaient atteints de tumeurs des voies urinaires supérieures. Alors que l'acquisition standard (T1W + T2W) a montré des performances diagnostiques insuffisantes, l'urographie par résonance magnétique (MRU) et l'imagerie pondérée par diffusion (DWI) ont présenté des scores de diagnostic élevés avec respectivement des sensibilités de 88,8 % et 94,0%, des spécificités de 88,1 % et 85,2 % et une précision du diagnostic de 83,0 % et 89,2 %. La DWI et le coefficient de diffusion apparent (ADC) semblent aussi être informatifs pour la stadification et l'évaluation pronostique.

Toutefois la littérature disponible sur les IRM des voies urinaires supérieures est maigre, les populations étudiées sont très hétérogènes, les designs très différents et des protocoles IRM très différents donnant des résultats très hétérogènes.

L'IRM présente un fort potentiel pour améliorer le diagnostic et la stadification des tumeurs des voies urinaires supérieures et permettrait ainsi d'améliorer la prise en charge et le traitement de nos patients. Malgré des données hétérogènes et des preuves limitées, les résultats de cette étude sont très encourageant et suggèrent que d'autres grandes études multicentriques devraient être menées afin de mieux évaluer les performances diagnostiques de l'IRM des voies urinaires supérieures, avec une acquisition standard prédéfinie (T1W, T2W, MRU, DWI avec une valeur de b ≥800, ADC).

Pour cela nous proposons un protocole de recherche clinique prospectif multicentrique afin de montrer l'intérêt de l'IRM dans le diagnostic des tumeurs de la voie excrétrice urinaire supérieure et de proposer une grille de lecture afin d'établir un UTi-RADS.

TITRE EN ANGLAIS : Up for UTi-RADS ? State of the art : a systematic review and meta-analysis.

DISCIPLINE ADMINISTRATIVE : Médecine spécialisée clinique

MOTS-CLÉS : UTi-RADS, diagnostic, pronostic, staging, IRM, voies excrétrices supérieures

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