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Upper tract imaging modality to investigate haematuria: cancer detection rates and changing guidelines

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Abstract

Background: To assess the imaging modalities used to investigate both visible haematuria and non-visible haematuria along with their detection rate of malignancy at two hospitals and the corresponding radiological workload produced.

Methods: A retrospective study was conducted across two hospitals. All CT urograms and ultrasound scans investigating haematuria in the outpatient setting over a 12-month period were evaluated.

Results: The detection rate for upper tract urothelial cancer with visible haematuria was 0.97% and for renal cell carcinoma was 0.64%. Of all the CT urograms performed for non-visible haematuria 4.9% had suspicious findings but none of these represents an underlying malignancy. Of all the ultrasound scans performed for either visible or non-visible haematuria, none were shown to have an underlying malignancy. The detection rate was thus zero for an upper tract urinary cancer or renal cell carcinoma in the non-visible haematuria group. A CT urogram was performed in 27% and 67% of cases in each respective hospital to further investigate non-visible haematuria. CT urography makes up 2.3% and 5.2% of each hospitals overall respective workload in the CT department. CT urography to investigate non-visible haematuria could be replaced by ultrasound in low-risk patients.

Conclusions: Radiological investigations are a limited resource and better rationalisation of upper tract imaging is needed in the setting of haematuria. Risk stratification of patients would be of benefit to help prevent a significant delay in timely diagnostics for higher risk individuals presenting with haematuria.

1 Background

Haematuria is one of the most common reasons for referral to the urology outpatient clinic accounting for up to 20% of referrals [1]. Haematuria is further sub-classified in to either visible haematuria (VH) or non-visible haematuria (NVH) the latter also being referred to as 'microscopic haematuria' or 'dipstick positive haematuria' although this terminology is no longer preferred. The main concern for either VH or NVH, especially in the absence of lower urinary tract symptoms, is its potential relation to urinary tract malignancy with VH more likely to herald a malignancy. VH is also associated with a higher stage of disease compared with NVH [2]. The investigations performed are thus to exclude a malignancy somewhere along the urinary tract. The upper tracts (kidneys and ureters) are imaged either by way of a CT urogram (CTU) or renal ultrasound (US) while the lower tracts (bladder, urethra) are visualised by way of a cystoscopy. The prostate is also assessed during cystoscopy for its size and vascularity as it can be a source of haematuria.

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A number of national organisations and specialty societies have released guidelines for the diagnosis and evaluation of haematuria. Existing guidelines vary in their definition of asymptomatic NVH (role of urine dipstick vs urine microscopy), the age threshold for recommending evaluation, as well as the optimal imaging method. While there is a general consensus amongst the various guidelines on the prompt investigation of VH, the investigation of NVH and in particular asymptomatic NVH is inconsistent [3]. The quoted incidence of a urological malignancy with both VH and NVH has changed over the last number of years in main stream text books. The second edition of the Oxford Handbook of Urology published in 2009 quotes a bladder cancer incidence rate of 34% for patients > 50 years presenting with VH [4]. This compares to a rate of 4–12% in patients > 45 years with VH in the latest 4th edition published in 2019 [5]. Similar rates of change are also quoted in the NVH group with incidence rates of up to 13% dropping to 1.6% in the > 50 years population and less than 1% in younger patients. These discrepancies in the incidence rates for bladder cancer are also reflected in the literature [6]. NVH has been shown to be a poor screening tool for bladder malignancy as is positive urine cytology with lead times for positive cytology and a positive NVH test of eight and three months, respectively [7].

The recent DETECT I trial has demonstrated that an US can be used as a safe alternative to CTU for investigating upper tracts in the setting of NVH [8]. This spares the patient a significant radiation dose, the need for intravenous contrast, provides a faster and more prompt method of evaluation as well as reducing the workload on radiology.

2 Methods

A retrospective study was conducted across two hospitals. All CTU and US scans investigating haematuria in the outpatient setting over a 12-month period were evaluated ($N=478$). Data regarding indication, date of referral, date of booking, date of scan, grade of doctor, patient risk factors, and scan results were recorded. The total number of CTU and US performed for urology outpatients were also recorded. Visible haematuria was defined as a visible sample of haematuria produced by the patient or a patient reported episode of visible haematuria. Non-visible haematuria was defined as +, ++ or +++ blood on urine dipstick and/or > 3 red blood cells per high power field on urine microscopy. The National Integrated Medical Imaging System (NIMIS) and the Picture Archive and Communication System (PACS) as well as patient charts and referral letters were used to source the required information. Data was evaluated using MS excel and IBM SPSS Version 24.

3 Results

The average age of patient was 60 years (25–83) in hospital 1 and 53 years (21–90) in hospital 2 with a sex distribution of 42% female ($n=201$) and 58% male ($n=277$). The average waiting time for a CTU was 58 and 124 days across the two hospitals with a lower average wait time for US of 38 and 62 days. US scans marked as 'urgent' were performed up to 3.5 times faster ($p<0.05$) in one institution than routine or unspecified time frames and CTUs performed up to 1.9 times faster ($p>0.05$). Table 1 outlines the breakdown of the imaging reports in to either 'No malignancy' or ' Suspicious' for a potential malignancy. Of the suspicious findings group for VH just over half (52%) of the suspicious CTUs had a confirmed malignancy while none of the suspicious US scans had a malignancy. For the NVH group none of the suspicious

Table 1 Clinical findings based on visible and non-visible haematuria presentations

	Hospital 1		Hospital 2	
	CT urogram	**Ultrasound**	**CT urogram**	**Ultrasound**
Visible haematuria	178	78	40	12
No malignancy	81.6% ($n=155$)	92.3% ($n=72$)	85.7% ($n=36$)	100% ($n=12$)
Suspicious findings	12.1% ($n=23$)	7.7% ($n=6$)	9.5% ($n=4$)	0
Malignancy confirmed	6.3% ($n=12$)	0	4.8% ($n=2$)	0
Non-visible haematuria	35	96	26	13
No malignancy	97.1% ($n=34$)	97.9% ($n=94$)	92.3% ($n=24$)	84.6% ($n=11$)
Suspicious findings	2.9% ($n=1$)	2.1% ($n=2$)	7.7% ($n=2$)	15.4% ($n=2$)
Malignancy confirmed	0	0	0	0
Total no. of scans performed	9,078	> 12,000	1,265	3,475
Total no. of scans for haematuria	213 (2.3%)	174	66 (5.2%)	25 (0.7%)

findings on either CTU or US demonstrated an underlying malignancy.

Combining the number of scans across the two hospitals of all the CTUs performed for VH 6.4% had a confirmed malignancy. Those with VH were 6.9 times ($p < 0.05$) more likely to have a positive finding on imaging and 12.5 times more likely to have an underlying malignancy ($p < 0.05$). Of the 14 malignancies identified nine were urothelial cancers of the bladder, three were upper tract urothelial cancer (UTUC) of the kidney and two were renal cell carcinoma (RCC). The detection rate for UTUC with VH was 0.97% and for RCC was 0.64%. Of all the CTUs performed for NVH only 4.9% were suspicious with none of these representing an underlying malignancy. Of all the US scans performed for either VH or NVH none were shown to have an underlying malignancy. The detection rate was thus zero for an UTUC or RCC in the NVH group.

4 Discussion

This study has shown that the use of radiological investigations as part of the workup for both VH and NVH are inconsistent across the two hospitals looked at in this study. The use of US, in the setting of VH to assess for upper tract pathology, is not recommended given its low sensitivity for UTUC of 14.3% with 85.7% sensitivity for a RCC [6]. However, US is performed in 29% of cases across both institutions for VH. Likewise the use of CTU may not be necessary given the findings of the DETECT I study to investigate upper tracts in the setting of NVH. A CTU was performed in 27% and 67% of cases in each respective hospital to further investigate NVH. Interestingly, CTUs to investigate haematuria make up 2.3% and 5.2% of each hospitals overall respective workload in the CT department. Further reductions in the number of CTUs performed would be a welcome reduction in workload for the radiology department as well sparing the patient the potential harmful sequela of a contrast enhanced scan of which they are often unaware [9].

Our study has also highlighted a significant issue regarding waiting times for both outpatient radiological investigations and outpatient appointments as well as large discrepancies in wait times despite both institutions being in the same hospital group. Table 2 highlights the mean wait times. For a CTU it was 58 days and 124 days, while for an US was 38 days and 62 days for Hospital 1 and Hospital 2, respectively. The longer waiting times in Hospital 2 was also identified with regard to outpatient appointments with a mean wait time of 528 days compared to 61 days in Hospital 1. It is the authors opinion that the large discrepancy in waiting times may be due, at least in part, to understaffing at hospital 2 at the time of this study. Current recommendations by the National Institute for Health and Care Excellence (NICE) state that if a referral meets their criteria, a urologist should see the patient within 14 days as a suspected cancer and if cancer is found treatment should be completed within 62 days [10]. Current Irish targets are < 28 days for urgent VH and NVH in adults over 50 years and < 13 weeks for semi-urgent NVH as set out in the latest urology model of care document [1].

There is a consensus amongst various guidelines that upper tracts need to be radiologically evaluated in the setting of haematuria. European Association of Urology (EAU) guidelines differ somewhat in interpretation as they are cancer specific rather than symptom specific and do not specify a recommendation for asymptomatic NVH like other guidelines. They do, however, state that 'visible haematuria was found to be associated with higher stage disease compared to non-visible haematuria'. The latest guidelines published in 2021 also states that US cannot reliably replace CTU to exclude UTUC [11]. The latest American Urological Association (AUA) guidelines published in 2020 now advocates

Table 2 Mean imaging and outpatient wait times

	Hospital 1		Hospital 2	
	CT Urogram	**Ultrasound**	**CT Urogram**	**Ultrasound**
Mean scan wait time (days)	58 (7–190)	38	124 (0–222)	62 (1–189)
Urgent	43	3	100	13
3 months	44	2	33	157
Immediate	55	N/A	N/A	N/A
Unspecified	72	29	126	47
Routine	74	0	188	N/A
Outpatient	116	4	141	94
Mean age	60 (25–90)	51 (21–87)	54 (19–90)	51 (21–79)
Mean OPD wait time (days)	61		522	

risk stratification of patients with NVH in to either low, intermediate or high-risk groups. Ultrasound is recommended to assess upper tracts in the low and intermediate groups and multiphasic CT urography for the high-risk group [12]. This differs to the 2016 guidelines which recommended the use of CT urography as part of the workup for all patients with NVH [13]. The latest Canadian guidelines, published in a consensus statement in 2016 [14], advocate the use of CTU for VH as well as symptomatic NVH, however, the radiological investigation of choice for asymptomatic NVH is at the discretion of the physician and patient on a case by case basis. Using US for investigating NVH would reduce CTUs by 15.7% and 38.8% in the hospitals of this study.

The most appropriate workup for NVH remains open to debate. In a recent meta-analysis by Jubber et al. of patients referred with NVH the pooled detection rate was 3.2% for bladder cancer, 0.042% for upper tract urothelial cancer, and 0.28% for kidney cancer [6]. These results would certainly challenge the need for any imaging of the upper tracts in low-risk patients. Nordic countries such as Sweden abandoned testing for asymptomatic NVH in 2002 with Denmark following suit in 2016. There is increasing interest in using a nomogram approach to guide the selection of patients with haematuria for evaluation. Incorporating the use of urinary biomarkers with nomograms, which has shown promising results [15, 16], may also play a role in the future as part of risk stratification in this group with earlier workup for higher risk patients. Further risk stratification of patients in the NVH group would be of benefit to help prevent a significant delay in timely diagnostics for higher risk individuals. This risk stratification approach has been recommended in the latest AUA guidelines as aforementioned. A simple pro forma to highlight higher risk patients used in the outpatient setting or even as part of a national referral form for general practice would be useful given the significant delays demonstrated in this study. Simply triaging referrals based on either visible or non-visible haematuria is not a sustainable method of triage. This study has shown what happens once referrals outnumber available resources leading to significant delays. The true 'at risk' patients do not emerge from the group as such, potentially leading to a delayed diagnosis with poorer outcomes.

Strengths of this study are its multi-institutional review for comparison of contemporary clinical practices. It provides up-to-date review of current international guidelines. This study also demonstrates the potential impact of changing clinical practice to the radiological workload of a hospital. Limitations of this study are moderate sample size and the limited further evaluation of patients with VH who only had an US performed as part of their workup.

5 Conclusions

Radiological investigations are a limited resource and better rationalisation of upper tract imaging is needed in the setting of haematuria. A risk stratification-based approach to patients presenting with NVH would allow better allocation of resources to higher risk patients in a more timely manner.

Abbreviations

VH: Visible haematuria; NVH: Non-visible haematuria; CTU: CT urogram; US: Ultrasound; NIMIS: National Integrated Medical Imaging System; PACS: Picture Archive and Communication System; UTUC: Upper tract urothelial cancer; NICE: National Institute for Health and Care Excellence; EAU: European Association of Urology; AUA: American Urological Association.

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Authors' contributions

All authors have read and approved the manuscript. LCY (Primary corresponding author) concept, design, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review. DM contributed to data acquisition and manuscript review. AW contributed to data acquisition and manuscript review. AR contributed to data acquisition and manuscript review. KP contributed to manuscript editing and manuscript review. RP contributed to manuscript editing and manuscript review.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study has complied with local ethical standards set down by Beaumont Ethics Committee, Beaumont Hospital, Dublin 8, Ireland. No identifiable patient data is presented in this study. As data was captured as part of a retrospective audit process individual patient consent was not required.

Consent for publication

Not applicable. No identifiable or individual data from patients was used in this study.

Competing interests

There are no competing interests to disclose.

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