Evaluation of the Risks and Benefits of CT Urography for Assessment of Gross Hematuria Todd Yecies, MD, Jathin Bandari, MD, Bruce Jacobs, MD, Benjamin Davies, MD University of Pittsburgh Medical Center Department of Urology

Introduction:

- Patients with gross hematuria are recommended to undergo CT Urography (CTU) due to increased sensitivity for detection of upper tract urothelial carcinoma (UTUC) and renal cell carcinoma (RCC) compared to renal ultrasound or IV urography.
- CTU is associated with high doses of ionizing radiation.
- The associated rates of radiation-induced malignancy and subsequent mortality remain unknown.
- The Biological Effects of Ionizing Radiation (BEIR) VII Phase 2 report provides a framework for estimating the lifetime attributable risk of cancer incidence and mortality associated with radiation exposure.
- The risk of malignancy due to ionizing radiation in the evaluation of microscopic hematuria is herein assessed applying the BEIR framework.

Methods:

- A PUBMED-based literature search was performed to identify model inputs, specifically detection rates of upper tract malignancy in gross hematuria patients stratified by age and gender, age and gender distribution of gross hematuria patients, sensitivity of renal ultrasound for detection of upper tract malignancy, loss of life expectancy from a secondary malignancy diagnosis, and CTU effective radiation dose.
- Estimates of radiation-induced secondary malignancy rates were obtained from the Biological Effects of Ionizing Radiation VII report with dose extrapolation using the linear no-threshold model.
- 1 and 2-way sensitivity analysis was performed to assess robustness of results to variable model inputs.

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| Model Input | | | | Sources | |
|------------------------------------|-----------------|------------|--------|---|--|
| | | UTUC | RCC | | |
| Prevalence of UTUC and RCC in | | | | Khadra et al., 2000, Edwards et | |
| gross hematuria patients | | 0.63% | 1.20% | al., 2006, Commander et al., 2017 | |
| | | | | Cauberg et al. 2011. Warshaur et | |
| Sensitivity of renal ultrasound | | 77% | 82% | al. 1988 [,] Jamis-Dow et al. 1996 | |
| Gross hematuria population | Age | Male | Female | Khadra et al., 2000 | |
| | <40 | 9.60% | 5.43% | | |
| | 40-49 | 8.56% | 3.86% | | |
| | 50-59 | 10.75% | 4.70% | | |
| | 60-69 | 17.33% | 5.95% | | |
| | >70 | 26.40% | 7.41% | | |
| Radiation dose from CTU | 31.7 mSv | | | Smith-Bindman et al., 2009 | |
| Lifetime attributable risk of | Age | Male | Female | BEIR VII Phase II Report | |
| secondary malignancy from 31.7 mSv | <40 | 0.201% | 0.265% | | |
| | 40-49 | 0.183% | 0.229% | | |
| | 50-59 | 0.142% | 0.182% | | |
| | 60-69 | 0.106% | 0.127% | | |
| | >70 | 0.054% | 0.066% | | |
| Loss of life expectancy from | Age | | | Baade et al., 2012 | |
| secondary malignancy | | 11.2 years | | | |
| | | 10.5 years | | | |
| | | 8.0 years | | | |
| | 60-69 6.0 years | | years | | |
| | | 3.9 years | | | |

Table 1: Model inputs and associated sources.

Abbreviations: UTUC, upper tract urothelial carcinoma; RCC, renal cell carcinoma; CTU, CT Urogram

| | Females age < 50 | Males age < 50 | Females age > 50 | Males age > 50 |
|--|------------------|----------------|------------------|----------------|
| Risk of upper tract malignancy | 0.28% | 0.79% | 1.41% | 2.57% |
| Risk of false negative ultrasound | 0.06% | 0.16% | 0.28% | 0.51% |
| Risk of CTU-induced malignancy | 0.25% | 0.19% | 0.11% | 0.08% |
| LLE from CTU (years) | 0.027 | 0.021 | 0.007 | 0.005 |
| Threshold LLE from undiagnosed upper tract malignancy at which CTU is superior to ultrasound (years) | 49.04 | 13.43 | 2.36 | 0.95 |

Table 2: Comparison of the risk of undiagnosed upper tract malignancy on renal ultrasound with the risk of radiation induced malignancy from CTU sub-stratified by age and gender. Abbreviations: CTU, CT Urogram; LLE, loss of life expectancy.



Figure 1: 1-way sensitivity analyses of loss of life expectancy (LLE) from undiagnosed upper tract malignancy identifying the threshold at which the LLE from CTU radiation exceeds the LLE from undiagnosed malignancy on RUS stratified by age and gender Abbreviations: CTU, CT Urogram; RUS, Renal Ultrasound.



Figure 2: 2-way sensitivity analyses performed as LLE from undiagnosed upper tract malignancy is varied from 1 to 3 years. Regions in red represent the frontier of inputs at which RUS is superior to CTU, while blue represents the range of inputs at which CTU is superior to RUS. Black lines represents model inputs as depicted in Table 1. Abbreviations: LLE, loss of life expectancy; CTU, CT Urogram; RUS, Renal Ultrasound.

Results:

Patients with gross hematuria have a prevalence of upper tract urothelial carcinoma and renal cell carcinoma of 0.63% and 1.2%, respectively. Male gender and age over 50 years were associated with a relative risk of upper tract malignancy of 2.04 and 2.95, respectively.

Renal ultrasound has a sensitivity of 77% for UTUC and 82% for RCC.

The estimated loss of life expectancy from a radiation-induced secondary malignancy ranged from 11.2 years in patients under 40 to 3.9 years in patients over 70.

Effective radiation dose of CTU was 31.7 mSv. Loss life expectancy from a missed diagnosis of upper tract malignancy is unknown.

The threshold value of this unknown above which the loss of life expectancy from CTU is less than the loss of life expectancy from ultrasound was identified (Table 2). This ranged from 49.04 years in females under 50 to 0.95 years in males over 50.

Conclusion:

This model suggests that in low-risk patients, CTU for evaluation of gross hematuria may carry a significant risk of radiation-induced secondary malignancy relative to the number of additional cases of upper tract malignancy detected.

