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2019

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### Recommended Citation

Liang, Brooke; Lange, Sara S.; Massad, L. Stewart; Dick, Rebecca; Mills, Kathryn A.; Hagemann, Andrea R.; McCourt, Carolyn K.; Thaker, Premal H.; Fuh, Katherine C.; Mutch, David G.; Powell, Matthew A.; and Kuroki, Lindsay M., "Do gynecologic oncology patients with severely diminished renal function and urinary tract obstruction benefit from ureteral stenting or percutaneous nephrostomy?" *Gynecologic Oncology Reports*. 28, 136-140. (2019).

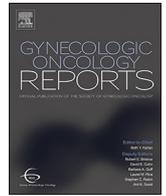
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## Case series

# Do gynecologic oncology patients with severely diminished renal function and urinary tract obstruction benefit from ureteral stenting or percutaneous nephrostomy?

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## ARTICLE INFO

## Keywords:

Urinary tract obstruction  
Gynecologic oncology  
Diuretic renal scintigraphy  
Ureteral stent  
Percutaneous nephrostomy tube

## ABSTRACT

**Objective:** To assess the renal outcomes of gynecologic oncology patients who present with hydronephrosis and acute kidney injury (AKI), have < 20% renal function on diuretic renal scintigraphy, and undergo placement of a ureteral stent or percutaneous nephrostomy (PCN) tube.

**Methods:** This is a single-institution case series of gynecologic oncology patients who underwent diuretic renal scintigraphy from January 1, 2007, to June 1, 2017. Univariate and multivariate logistic analyses were used to assess predictors of < 20% renal function. Recovery from AKI or elevated creatinine was reported for women with < 20% renal function who received a unilateral ureteral stent or PCN tube on the same side as their more compromised kidney.

**Results:** Among 353 gynecologic oncology patients who underwent diuretic renal scintigraphy, 58 (16%) had renal function < 20%. Mean age was 59.6 years, 17% had preexisting chronic kidney disease, and 44% had a diagnosis of cervical cancer. Renal atrophy on computed tomography scan (aOR 18.24, 95% CI 1.21–274.92) predicted renal function < 20%. Of 10 women with < 20% renal function who received a stent or PCN tube, 7 recovered from AKI or elevated creatinine.

**Conclusions:** Gynecologic oncology patients with < 20% renal function may recover from AKI after placement of a stent or PCN tube, indicating that a diuretic renal scintigraphy cutoff of < 20% renal function may be overly conservative. Future studies are warranted to determine optimal renal function cutoffs for stent/PCN tube placement in gynecologic oncology patients.

## 1. Introduction

Gynecologic oncology patients commonly experience urinary tract obstruction due to tumor extension, metastatic growth, or radiation therapy (Shingleton et al., 1969). Upon detecting such obstructions, providers must decide whether or not to recommend placing a ureteral stent or percutaneous nephrostomy (PCN) tube. Although such procedures might prevent acute kidney injury (AKI) and improve overall morbidity and mortality (Lienert et al., 2009; Patel et al., 2015), they could be futile when kidney function is too impaired.

A valuable method for assessing kidney function is diuretic renal

scintigraphy. In contrast to ultrasound and other renal imaging, this nuclear medicine imaging study assesses both ureteral obstruction and renal function in a single test. Renal scintigraphy measures the speed of radiotracer clearance through the urinary tract after diuretic administration. Clearance is rapid in a non-obstructed system, but slow or entirely stagnant in an obstructed system. A further advantage of renal scintigraphy is that it can quantify differential excretion times of the two kidneys and calculate the percent contribution of each kidney to the patient's total renal function.

According to the urology literature, diuretic scintigraphy revealing  $\geq 20\%$  kidney function is the generally accepted threshold of kidney

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<https://doi.org/10.1016/j.gore.2019.04.007>

Received 9 January 2019; Received in revised form 19 April 2019; Accepted 22 April 2019

Available online 24 April 2019

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salvageability (Ganatra and Loughlin, 2005; Klaipetch et al., 2013; KDIGO, 2012; Xu et al., 2017). If kidney function is less than this cutoff, placement of a ureteral stent or PCN tube is likely to be futile. However, no studies have assessed the validity of this cutoff in a gynecologic oncology patient population. Given that such patients' cancer treatment options (e.g., chemotherapy, immunotherapy, radiosensitizing agents) may depend on renal function, it is important to determine whether the 20% cutoff is appropriate in this population.

To address this question, we retrospectively analyzed a case series of gynecologic oncology patients at our institution who presented with hydronephrosis and AKI and underwent renal scintigraphy. Specifically, our objective was to determine the rate of recovery from kidney injury in patients who underwent ureteral stenting or PCN on the same side as their more compromised kidney. Additionally, because diuretic renal scintigraphy may not be available to all gynecologic oncologists, we sought to describe clinicodemographic predictors of < 20% renal function.

## 2. Methods

This was a single-institution retrospective case series of all gynecologic oncology patients who underwent diuretic renal scintigraphy between January 1, 2007, and June 1, 2017. Before study initiation, all study procedures were reviewed and approved by the Washington University Human Research Protection Office (Institutional Review Board project # 201708045).

Patients were identified by querying the Barnes-Jewish Hospital (BJH) Nuclear Medicine database for inpatient and outpatient diuretic renal scintigraphy tests ordered within the Division of Gynecologic Oncology. We included patients with cervical, endometrial, ovarian/fallopian/peritoneal, vaginal, or vulvar cancer, as well as gestational trophoblastic disease, and those with a cancer of unknown but assumed gynecologic origin. If multiple diuretic renal scintigraphy tests were performed during the same hospitalization or AKI work-up, only the initial scan result was included in our analysis.

Diuretic renal scintigraphy was performed at our institution as follows: Patients were first hydrated with 500 ml of water orally and 500 ml of normal saline infused intravenously over 30 mins starting 15 mins before the procedure. Next, they were intravenously administered 7.5 mCi of Technetium Mertiactide (Tc-99m MAG3). Patients were then asked to void, and 2–4 mins of baseline data were acquired. Twenty minutes after Tc-99m MAG3 administration, 40 mg of the diuretic furosemide was given intravenously over 1–2 mins, and data were acquired continuously for 20 mins after furosemide administration.

AKI was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria: serum creatinine increase by 0.3 mg/dl in 48 h or by 1.5-fold in 7 days (KDIGO, 2012). Other elevations in serum creatinine noted by clinicians that did not meet criteria were captured and classified as “elevated creatinine”. Development of chronic kidney disease (CKD) after AKI was defined according to the KDIGO criteria: presence of kidney damage or decreased glomerular filtration rate < 60 ml/min/1.73 m<sup>2</sup> for 3 or more months (KDIGO, 2012). Failure to salvage was defined as a serum creatinine that did not return to within 25% of baseline by 3 months after the procedure or death due to AKI (Pannu et al., 2013).

We extracted demographic and clinicopathologic data including age at diuretic renal scintigraphy, race, insurance, tobacco use, comorbidities, primary cancer type, cancer stage, indication for diuretic renal scintigraphy, and documented renal findings on computed tomography (CT) scan (e.g., renal atrophy, cortical thinning, or hydronephrosis/hydronephrosis) as reported by the BJH radiology department. Renal interventions (e.g., ureteral stents and/or PCN tubes) and outcomes were captured.

Standard descriptive statistics including median and interquartile range for continuous variables, and count and percentage for

categorical variables, were used to summarize demographic/clinicopathologic characteristics, stent/PCN placement, and renal outcomes. Mann-Whitney U or Student's *t*-test were used to analyze significance in continuous variables, and Fisher's Exact or  $\chi^2$  tests were used for categorical variables.

Univariate and multivariate logistic regression models were used to assess predictors of < 20% renal function. The predictors that were significantly different between groups in bivariate analysis with a significance level of 0.05 (renal atrophy on CT scan, prior pelvic/abdominal radiation, and AKI satisfying KDIGO criteria) were controlled for in a logistic regression model. Stata 15 (Stata Statistical Software, Release 15, College Station, TX) was used for all analyses.

## 3. Results

Our query of the nuclear medicine database yielded 420 diuretic renal scintigraphy tests ordered by the gynecologic oncology division between January 1, 2007, and June 1, 2017. 353 diuretic renal scintigraphy tests remained after patients with benign diagnoses were excluded and extra scans ordered within the same hospitalization or AKI work-up were removed. Of the 353 test results, 58 (16%) revealed < 20% renal function. Of the patients with < 20% renal function, mean age was 57.2, and most were insured, non-obese, white patients with advanced or recurrent gynecologic malignancy, most often cervical cancer (Table 1).

Among women with < 20% renal function, indications for diuretic renal scintigraphy were mainly the provider's suspicion for hydronephrosis/hydronephrosis (84%) and/or elevated creatinine or suspected AKI (55%). Providers ordered multiple imaging studies in tandem with diuretic renal scintigraphy; 4 (7%) patients had a renal ultrasound and 34 (58%) had a CT scan performed within 30 days before diuretic renal scintigraphy. Compared to patients with  $\geq$ 20% renal function, those with < 20% renal function were more likely to have renal atrophy on CT scan (13 [19%] vs. 6 [2%],  $P < .01$ ).

Predictors of < 20% renal function were evaluated in univariate and multivariate models (Table 2). After adjusting for potential confounders, renal atrophy diagnosed on CT scan (adjusted odds ratio [aOR] 18.24, 95% confidence interval [CI] = 1.21–274.92) was associated with < 20% renal function.

We examined the subgroup of women with AKI or elevated creatinine and < 20% renal function on diuretic renal scintigraphy who received a unilateral stent/PCN for their more compromised kidney. Of the 10 patients in this group, 7 recovered from their AKI/elevated creatinine and 3 did not. Among the 7 patients who recovered, median (range) serum creatinine improved from 1.2 (1.08–1.43) mg/dl at AKI/elevated creatinine diagnosis to 0.82 (0.75–0.90) mg/dl. Based on the last serum creatinine measurements available at the time of data acquisition, these patients continued to have normal renal function for a median of 13.1 (0.2–77.4) months. Table 3 describes the renal and survival outcomes of women in this subgroup.

## 4. Discussion

In our case series of gynecologic oncology patients with < 20% renal function detected by diuretic renal scintigraphy, the majority of those who underwent stent or PCN placement recovered from AKI or elevated creatinine (7 out of 10). Although this conclusion is based on a small sample size, it suggests that, contrary to reports in the urology literature (Xu et al., 2017; Ortapamuk et al., 2003), 20% renal function is not a reliable cutoff for defining kidney salvageability in gynecologic oncology patients. If this conclusion is confirmed in additional studies, it has strong implications for our patient population whose treatment options (e.g., chemotherapy, immunotherapy, radiosensitizing agents) may depend on maintaining some degree of renal function. A prospective, multicentered study is needed to determine the optimal renal function threshold for predicting whether or not gynecologic oncology

**Table 1**  
Demographic and clinicopathologic characteristics.

Characteristic	n (%)			P
	Total	< 20% Renal function	≥ 20% Renal function	
	N = 353	N = 58	N = 295	
Age (years)		57.2 (45.3–66.5)	60.27 (50.1–69.0)	0.07
BMI (kg/m <sup>2</sup> )				0.44
< 30	207 (59)	37 (64)	170 (58)	
30–39.9	103 (29)	14 (24)	89 (30)	
40–49.9	33 (9)	4 (7)	29 (10)	
≥ 50	10 (3)	3 (5)	7 (2)	
Race				0.41
White	260 (74)	45 (77)	215 (73)	
Black	84 (24)	13 (22)	71 (24)	
Other	8 (2)	0 (0)	8 (3)	
Insurance				0.54
Uninsured	33 (9)	6 (10)	27 (9)	
Medicare/Medicaid	163 (46)	23 (40)	140 (48)	
Private	156 (44)	29 (50)	127 (43)	
Tobacco use				0.24
Never	218 (62)	31 (53)	187 (63)	
Former	67 (19)	13 (22)	54 (18)	
Current	66 (19)	13 (22)	53 (18)	
Charleston Comorbidity Score		6.5 (4.0–8.0)	7 (6.0–8.0)	0.18
Diabetes	57 (16)	9 (15)	48 (16)	0.89
Cardiac disease	181 (51)	30 (52)	151 (51)	0.94
Chronic kidney disease	61 (17)	14 (24)	47 (16)	0.13
Prior abdominal or pelvic radiation	160 (45)	33 (57)	127 (43)	0.05
Gynecologic cancer type				0.59
Cervical cancer	155 (44)	28 (48)	127 (43)	
Endometrial cancer	89 (25)	15 (26)	74 (25)	
Ovarian/fallopian/primary peritoneal cancer	102 (29)	15 (26)	87 (29)	
Vulvar/vaginal cancer	7 (2)	0 (0)	7 (2)	
Stage				0.08
I-II	117 (33)	14 (24)	103 (35)	
III-IV	206 (58)	40 (69)	166 (56)	
Recurrent disease	185 (52)	31 (53)	154 (52)	0.86
Number of chemotherapy regimens received				0.80
1st line	120 (34)	24 (41)	96 (33)	
2nd line	50 (14)	7 (12)	43 (15)	
3rd line	32 (9)	5 (9)	27 (9)	
> 3rd line	35 (10)	6 (10)	29 (10)	

Legend: BMI = body mass index; AKI: Acute kidney injury (defined as serum creatinine increase by 0.3 mg/dl in 48 h, or by 1.5-fold in 7 days); Cr: Creatinine; CT: computed tomography; PCN: percutaneous nephrostomy tube. Data are median (IQR), or n (%) unless otherwise specified. Missing values were included in denominator of the percentages.

**Table 2**  
Predictors of < 20% renal function as detected by diuretic renal scintigraphy.

Risk factor	Univariate	Multivariate
	uOR (95% CI)	aOR (95% CI)
Renal atrophy on CT scan	10.78 (3.74–31.10)	18.24 (1.21–274.92)
Prior abdominal or pelvic RT	1.75 (0.99–3.08)	0.86 (0.08–8.82)
AKI	0.27 (0.09–0.77)	0.08 (0.001–4.90)

Legend: CT: computed tomography; RT: radiation therapy; CKD: chronic kidney disease, AKI: acute kidney injury (defined as serum creatinine increase by 0.3 mg/dl in 48 h, or by 1.5-fold in 7 days); uOR = unadjusted odds ratio; aOR = adjusted odds ratio; CI = confidence interval.

patients will benefit from a stent or PCN tube.

Because diuretic renal scintigraphy may not be available to all

gynecologic oncologists, we analyzed predictors of < 20% renal function in our case series of 353 gynecologic oncology patients who underwent diuretic renal scintigraphy. Renal atrophy on CT scan was a strong, independent predictor of < 20% function on renal scintigraphy. Thus, we conservatively recommend that gynecologic oncology patients with suspected hydronephrosis/hydronephrosis and no renal atrophy detected on a CT scan can forego diuretic renal scintigraphy and proceed directly to ureteral stenting/PCN tube placement. However, those with renal atrophy on CT scan should undergo diuretic renal scintigraphy to quantify their renal function. Those with renal function over 20% should undergo ureteral stenting/PCN tube placement. Patients with renal function < 20% should discuss with their provider the utility of renal interventions. Such conversations should include the potential risks of ureteral stent/PCN tube placement (e.g., recurrent infection, tube dislocation or stent migration, and/or patient discomfort (Lienert et al., 2009)) and their associated healthcare costs. See Fig. 1 for our proposed algorithm for the workup for gynecologic oncology patients with AKI or elevated creatinine and suspected hydronephrosis/hydronephrosis.

Strengths of this study include its unique focus on diuretic renal scintigraphy in gynecologic oncology patients. While there is literature involving management of upper urinary tract obstruction(s) in cancer patients, there remain gaps in knowledge regarding the impact diuretic renal scintigraphy can have on tailoring renal interventions and subsequent outcomes including renal function, survival, and quality of life. Additionally, instead of using surrogate renal function measures such as CKD or hemodialysis, we used objective renal function data from diuretic renal scintigraphy. Important weaknesses of our study include the small sample size drawn from a single institution and the retrospective study design, which may have been subject to selection bias. Thus, our findings may not be generalizable. Additionally, diuretic renal scintigraphies were ordered at the providers' discretion and were rarely repeated after stent or PCN placement to assess recovery of renal function. Therefore, we could only infer utility of the interventions from patients' diagnoses of AKI or elevated creatinine. Despite these limitations, the results of our study may help gynecologic oncology patients and providers decide whether or not to place a ureteral stent(s) or PCN tube(s).

In conclusion, we have shown that among gynecologic oncology patients, independent predictors of < 20% renal function include renal atrophy observed on CT scan. Twenty percent relative renal function on diuretic renal scintigraphy may not be an appropriate cutoff for kidney salvageability in gynecologic oncology patients, as the majority of our patients who underwent ureteral stent/PCN tube placement had improved renal outcomes. Thus, we recommend an individualized approach for those with severely compromised renal function, including discussion of potential risks, benefits, and quality of life. Future studies are warranted to determine optimal renal function cutoffs for stent/PCN tube placement in gynecologic oncology patients.

## Conflict of interest

Dr. McCourt reports Genentech Speaker's Bureau and UpToDate Ad Hoc section editor for endometrial cancer. Dr. Thaker reports personal fees from Celsion, personal fees from Stryker, grants and personal fees from Tesaro, grants and personal fees from Merck, personal fees from Abbvie, personal fees from Clovis, outside the submitted work. Dr. Powell reports personal fees from Merck, personal fees from Tesaro, personal fees from Clovis Oncology, personal fees from AstraZeneca, personal fees from Roche/Genentech, personal fees from GOG Foundation, outside the submitted work. Dr. Kuroki reports grants from Washington University Institute of Clinical and Translational Sciences (R25 STRENGTH and KL2) during the conduct of the study. All other authors declare no potential conflict of interest.

**Table 3**  
Subgroup report on women with AKI or elevated creatinine and < 20% renal function on diuretic renal scintigraphy who received a unilateral stent/PCN for their more compromised kidney.

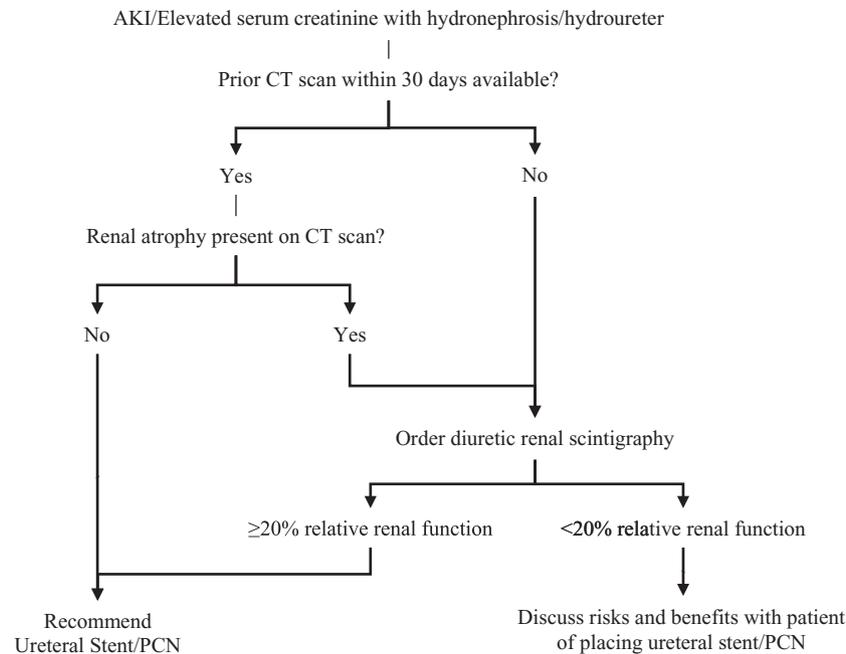
Recovery from AKI or elevated creatinine <sup>a</sup>	Age at AKI / elevated creatinine diagnosis (years)	Primary cancer	Stage	Recurrence	Baseline serum creatinine (mg/dl)	Serum creatinine at AKI / elevated creatinine diagnosis (mg/dl)	Serum creatinine after stent / PCN (mg/dl) <sup>b</sup>	Duration of sustained normal creatinine after stent / PCN (mo) <sup>c</sup>	Patient Outcome	Survival (mo)
Recovered	65	Endometrial	IV	No	0.81	1.13	0.9	1.6	Dead of cancer	2.9
Recovered	71	Cervical	III	No	Unknown	1.2	0.81	1.8	Dead of cancer	2.6
Recovered	52	Cervical	II	No	1.05	1.43	0.75	77.4	Alive with cancer	≥ 96.0
Recovered	59	Endometrial	IV	No	0.7	1.08	0.83	28.7	Alive NED	65.4
Recovered	62	Endometrial	Unknown	Yes	0.89	1.14	0.82	0.2	Dead of cancer	1.7
Recovered	59	Endometrial	IV	Yes	1.1	1.22	0.82	14.4	Dead of cancer	15.4
Recovered	78	Ovarian	III	No	0.9	1.23	0.85	13.1	Alive NED	≥ 31.4
Did not recover	62	Endometrial	IV	No	Unknown	1.9	1.4	n/a	Dead of cancer	15.1
Did not recover	50	Ovarian	IV	Yes	1.06	1.53	1.6	n/a	Lost to follow up	Unknown
Did not recover	73	Endometrial	IV	Yes	0.65	1.5	1.24	n/a	Dead of cancer	55.4

Legend: AKI: acute kidney injury (defined as serum creatinine increase by 0.3 mg/dl in 48 hours, or by 1.5-fold in 7 days).

<sup>a</sup> Recovery defined as serum creatinine that returned within 25% of baseline by 3 months (8)

<sup>b</sup> Serum creatinine reported at approximately 3 months post-stent or post-PCN

<sup>c</sup> Based on availability of serum creatinine records. Normal serum creatinine defined by institutional laboratory as 0.60-1.10 mg/dl



**Fig. 1.** Algorithm for work-up of AKI or elevated creatinine in gynecologic oncology patients with suspected hydronephrosis/hydronephrosis.

Legend: AKI: acute kidney injury (defined as serum creatinine increase by 0.3 mg/dl in 48 h, or by 1.5-fold in 7 days); CT: computed tomography; PCN: percutaneous nephrostomy.

#### Author contributions

1. Brooke Liang, B.S.: Lead author who performed the majority of data collection and entry, and assisted with manuscript writing.
2. Sara S. Lange, M.D.: Performed data collection and entry, as well as assisted with manuscript writing and revisions.
3. L. Stewart Massad, M.D.: Involved with conception and study design. Assisted with manuscript revisions and approval of final submitted version.
4. Rosa Schulz, M.P.H.: Assisted with statistical analysis and approval of final submitted version.
5. Kathryn A. Mills, M.D.: Performed data collection and entry, as well as assisted with manuscript revisions and approval of final submitted version.
6. Andrea R. Hagemann, M.D., M.S.C.I: Assisted with manuscript revisions and approval of final submitted version.
7. Carolyn K. McCourt, M.D.: Assisted with manuscript revisions and approval of final submitted version.
8. Premal H. Thaker, M.D., M.S.: Assisted with manuscript revisions and approval of final submitted version.
9. Katherine C. Fuh, M.D., Ph.D.: Assisted with manuscript revisions and approval of final submitted version.
10. David G. Mutch, M.D.: Assisted with manuscript revisions and approval of final submitted version.
11. Matthew A. Powell, M.D.: Assisted with manuscript revisions and approval of final submitted version.
12. Lindsay M. Kuroki, M.D., M.S.C.I: Senior author who helped with initial design, IRB submission, data entry, and manuscript writing.

#### Acknowledgements

We would like to thank Deborah Frank, PhD for critically reviewing

this manuscript and assisting with scientific editing. Research reported in this publication was supported by the Washington University Institute of Clinical and Translational Sciences grant UL1 TR000448 and R25CA190190 (PI, Dr. Bradley Evanoff) from the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

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