Adverse Urinary System Diagnoses among Older Women with Endometrial Cancer

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ABSTRACT

Background: Endometrial cancer and its treatment may impact urinary system function, but few large-scale studies have examined urinary diagnoses among endometrial cancer survivors. We investigated the risk of several urinary outcomes among older women with endometrial cancer compared with similar women without a cancer history.

Methods: Women aged 66+ years with an endometrial cancer diagnosis during 2004–2017 ($N = 44{,}386$) and women without a cancer history ($N = 221{,}219$) matched 1:5 on exact age, race/ethnicity, and state were identified in the Surveillance, Epidemiology, and End Results-Medicare linked data. ICD-9 and -10 diagnosis codes were used to define urinary outcomes in the Medicare claims. HRs for urinary outcomes were estimated using multivariable Cox proportional hazards regression models.

Results: Relative to women without cancer, endometrial cancer survivors were at an increased risk of several urinary system diagnoses, including lower urinary tract infection [HR, 2.36; 95% confidence interval (CI), 2.32–2.40], urinary calculus (HR, 2.22; 95% CI, 2.13–2.31), renal failure (HR, 2.28; 95% CI, 2.23–2.33), and chronic kidney disease (HR, 1.85; 95% CI, 1.81–1.90). Similar associations were observed in sensitivity analyses limited to 1+ and 5+ years after endometrial cancer diagnosis. Black race, higher comorbidity index, higher stage or grade cancer, non-endometrioid histology, and treatment with chemotherapy and/or radiation were often significant predictors of urinary outcomes among endometrial cancer survivors.

Conclusions: Our results suggest that, among older women, the risk of urinary outcomes is elevated after endometrial cancer.

Impact: Monitoring for urinary diseases may be a critical part of long-term survivorship care for older women with an endometrial cancer history.

Introduction

An estimated 66,570 new cases of endometrial cancer were diagnosed in the U.S. in 2021 (1), with nearly half (∼45%) among women aged 65 years and older (2). Most women (>80%) with endometrial cancer are expected to survive at least 5 years beyond their diagnosis (2). High 5-year survival, combined with an increase in incidence of about 1% per year since the mid-2000s (1), have led to a rapidly growing population of U.S. endometrial cancer survivors. By the year 2030, the number of women with an endometrial cancer history is predicted to exceed 1 million (3). This projected growth intensifies the need for survivorship-focused research to improve long-term health outcomes after endometrial cancer.

Primary treatment for endometrial cancer generally involves surgery (hysterectomy with or without bilateral salpingo-oophorectomy), often combined with radiotherapy in the form of vaginal brachytherapy or external beam radiation (4). In some women, exposure to these therapies may adversely impact urinary system function, leading to additional medical care needs and reduced quality of life in the posttreatment period (5–8). To date, however, few large-scale studies have attempted to quantify the incidence of specific urinary outcomes after endometrial cancer, or to assess how risk differs between endometrial cancer survivors and cancer-free women. A better understanding of patterns of urinary system diseases among women with endometrial cancer may help to anticipate the long-term care needs of the growing population of survivors.

In this study, our objective was to examine the risk of adverse urinary outcomes among older women with an endometrial cancer diagnosis. Using linked cancer registry records and Medicare claims data, we estimated the cumulative incidence of common urinary diseases among endometrial cancer survivors and compared the risk of these outcomes between women with and without an endometrial cancer history.

Materials and Methods

Data source and study cohort

Our study cohort was identified using data from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data resource. The SEER program is a system of population-based cancer registries that collects and reports data on cancer incidence and survival. These registries are located strategically across the U.S. and currently cover approximately 48% of the total U.S. population. Patient information collected by SEER registries includes patient demographic information, primary tumor site and morphology, stage at diagnosis, first course of treatment, vital status, and cause of death (9). Medicare is the federally funded health insurance program for individuals aged 65 and older and those under 65 with specific disabilities. Part A of Medicare covers inpatient hospital and skilled-nursing facility care, while Part B covers physician and outpatient services. Medicare data are linked to SEER records every two years using social security number, date of birth, name, and sex (10). For our analyses, we used SEER data from

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Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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2004 to 2017 linked to Medicare data from 2003 to 2018. This study was considered exempt by the University of North Carolina Institutional Review Board.

From the SEER-Medicare data, we identified women with a first primary endometrial cancer (sites C54.0-C54.9, C55.9) at ages 66 years and older between 2004 and 2017. Women were required to have at least 1 year of continuous enrollment in Parts A and B of Medicare prior to their endometrial cancer diagnosis date for identification of preexisting urinary system diseases and other comorbid conditions. Those diagnosed by death certificate or autopsy and those enrolled in a managed care plan in the month of or the year before diagnosis were excluded. Each woman with endometrial cancer was matched on year of birth, state of residence, and race/ethnicity (White, Black, Asian, Hispanic, Native American, other, unknown) to a maximum of 5 women without cancer from the random 5% sample of Medicare beneficiaries without a known history of cancer (11). We defined an index date for each matched set as the cancer diagnosis date of the endometrial cancer case included in that set.

Outcomes

Study outcomes were defined using ICD-9 and ICD-10 diagnosis codes in any position in the Medicare inpatient, outpatient, and physician/supplier claims. Primary outcomes included renal failure, chronic kidney disease (CKD), glomerular diseases, calculus of the urinary tract, other diseases of the kidney and ureter, lower urinary tract infections (UTI), diseases of the bladder, and diseases of the urethra (codes provided in Supplementary Table S1). Follow-up for outcomes began at the index date and ended at diagnosis of the outcome of interest, death, disenrollment from Medicare parts A or B, or end of follow-up in December 2018, whichever occurred first. Women with a diagnosis code for a specific urinary outcome within the year prior to the index date were considered to have prevalent disease and were not considered to be at risk for an incident outcome during follow-up.

Covariates

From the Medicare enrollment files, we abstracted information on age at diagnosis (or index date), race/ethnicity, state of residence, and date of death. State information was used to define four geographic regions (Midwest, Northeast, South, West). We used the Klabunde adaptation of the Charlson comorbidity index to define comorbidity status in the year prior to the index date (12, 13). The rule-out option, which requires that a diagnosis occur on two separate claims >30 days apart, was used to determine comorbidity status for this index (14). For women with endometrial cancer, cancer-related characteristics

Table 1. Demographic characteristics of women with endometrial cancer and matched women without cancer.

	Endometrial cancer (*N* = 44,386)		No cancer group (*N* = 221,219)	
	N	**%**	***N***	**%**
Age at diagnosis/index date				
66–69	12,034	27%	60,271	27%
70–74	12,410	28%	61,918	28%
75–79	8,910	20%	44,278	20%
80–84	6,028	14%	29,945	14%
85+	5,004	11%	24,807	11%
Median (IQR)	73	(69, 79)	73	(69, 79)
Race/ethnicity				
White	37,756	85%	188,723	85%
Black	4,182	9%	20,762	9%
Other	781	2%	3,795	2%
Asian	797	2%	3,899	2%
Hispanic	564	1%	2,671	1%
North American Native	108	0%	450	0%
Unknown	198	0%	919	0%
Region				
Midwest	4,198	9%	20,894	9%
Northeast	20,810	47%	103,820	47%
South	6,620	15%	32,932	15%
West	12,758	29%	63,573	29%
Charlson score				
0	17,031	38%	126,293	57%
1	11,530	26%	40,060	18%
2+	15,825	36%	54,866	25%
Prevalent urinary system diseases at index date[a]				
Acute and unspecified renal failure	1,881	4%	5,853	3%
CKD	3,396	8%	11,263	5%
Glomerular diseases	389	1%	1,209	1%
Calculus of the urinary tract	1,214	3%	2,935	1%
Other diseases of the kidney and ureter	4,615	10%	12,564	6%
Lower UTI	13,502	30%	34,592	16%
Diseases of the bladder	1,223	3%	3,642	2%
Diseases of the urethra	576	1%	1,076	0%

[a]Defined by at least one claim with a code for that condition in the year prior to the index date.

extracted from the SEER data included summary stage, histology, and grade. Both the SEER data and the Medicare claims were used to identify cancer treatments. Women were considered to have received a particular treatment type if they had a claim with a relevant code (Supplementary Table S2) within the year following cancer diagnosis or if the SEER data indicated they had received that treatment type as part of their first course of treatment.

Statistical analysis

We estimated the cumulative incidence of urinary outcomes among women with and without endometrial cancer using models that accounted for death as a competing risk. Multivariable Cox proportional hazards models were used to estimate HRs for urinary outcomes, comparing women with endometrial cancer to matched women without cancer. All models were adjusted for age at the index date, race/ethnicity, geographic region, and Charlson score. In sensitivity analyses, we began follow-up at 1 year and 5 years after the index date, to address the potential for increased urinary system diagnoses among endometrial cancer survivors due to increased medical surveillance within the first few years after cancer diagnosis.

Among women with endometrial cancer, multivariable Cox proportional hazards models were used to examine associations between demographic and cancer-related characteristics and urinary outcomes. *P* values for trend for age at cancer diagnosis and Charlson score were estimated using these characteristics as continuous variables. Analyses of associations with cancer treatments began follow-up at 1 year and 5 years after endometrial cancer diagnosis and correspondingly required 1 year and 5 years, respectively, of continuous Medicare Parts A and B enrollment after diagnosis. For analyses of associations with other pre- or at-diagnosis characteristics, follow-up began at diagnosis and did not require a specific duration of post-diagnosis continuous enrollment.

Data availability

The data analyzed in this study were obtained from the NCI.

Results

A total of 44,386 women with endometrial cancer and 221,219 matched women without cancer were included in our analyses. Women with endometrial cancer tended to have a higher Charlson comorbidity index and a higher prevalence of most urinary system diseases at the index date than women without cancer (**Table 1**). Cancer-related characteristics among women with endometrial cancer are shown in **Table 2**. Most women had localized stage disease (65%), endometrioid histology (69%), and grade 1 or 2 disease (62%). Overall, the most common treatment type was hysterectomy only (44%), followed by hysterectomy and radiation (20%).

Approximately one third (32%) of endometrial cancer survivors were diagnosed with a lower UTI within the year after the index date, with the cumulative incidence rising to 56% and 68% by 5 and 10 years, respectively (**Fig. 1**). Other common urinary outcomes after endometrial cancer included renal failure (1 year, 11%; 5 years: 24%), CKD (1 year, 7%; 5 years, 20%), and other diseases of the kidney and ureter (1 year, 21%; 5 years, 38%). Less common outcomes included diseases of the bladder (1 year, 4%; 5 years, 10%), calculus of the urinary tract (1 year, 3%; 5 years, 8%), glomerular diseases (1 year, 1%; 5 years, 3%), and diseases of the urethra (1 year, 1%; 5 years, 3%). For all study outcomes, the cumulative incidence among endometrial cancer survivors exceeded that among the matched comparison group (**Fig. 1**).

Table 2. Cancer characteristics among women with endometrial cancer ($N = 44{,}386$).

	N	%
Stage		
Localized	27,434	65%
Regional	9,899	24%
Distant	4,559	11%
Unknown/unstaged	2,494	
Histology		
Endometrioid	30,625	69%
Serous	4,142	9%
Carcinosarcoma	3,021	7%
Clear cell	881	2%
Mixed	2,841	6%
Other	2,876	6%
Grade		
1	11,596	33%
2	10,001	29%
3	9,420	27%
Undifferentiated	3,723	11%
Unknown	9,646	
Hysterectomy		
No	6,264	14%
Yes	38,122	86%
Chemotherapy		
No	33,265	75%
Yes	11,121	25%
Radiation		
No	27,549	62%
Yes	16,837	38%
Treatment		
Hysterectomy only	19,081	43%
Hysterectomy + radiation	9,138	21%
Hysterectomy + chemotherapy	4,088	9%
Hysterectomy + radiation + chemotherapy	5,815	13%
Chemotherapy and/or radiation	3,647	8%
No chemo, radiation, or hysterectomy	2,617	6%

In multivariable-adjusted models, women with endometrial cancer had an increased risk of all urinary outcomes examined relative to matched women without cancer (**Table 3**). HRs ranged from 1.85 (95% CI, 1.81–1.90) for CKD to 3.06 (95% CI, 3.00–3.12) for other diseases of the kidney and ureter. These associations largely persisted in analyses that started follow-up at 1 year and 5 years after the index date, though magnitudes of the HRs tended to be somewhat attenuated compared with primary analyses (Supplementary Table S3).

Among endometrial cancer survivors, the risk of most urinary outcomes tended to be higher among women who were older at cancer diagnosis (**Table 4**). Black women were at elevated risk of several outcomes, including renal failure, CKD, glomerular disease, and other diseases of the kidney/ureter, relative to White women. For example, the risk of renal failure among Black women was 1.75 times that of White women (95% CI, 1.61–1.84). Across other race/ethnicity groups, Hispanic women had an increased risk of lower UTIs relative to White women (HR = 1.17; 95% CI, 1.00–1.37).

Risk of urinary outcomes increased consistently with Charlson comorbidity index. In analyses according to cancer-related characteristics, women with higher stage disease tended to have higher risks of urinary diagnoses (**Table 4**). Higher grade was associated with higher risk of some outcomes, particularly renal failure and other diseases of the kidney/ureter. Associations with histology were less consistent.

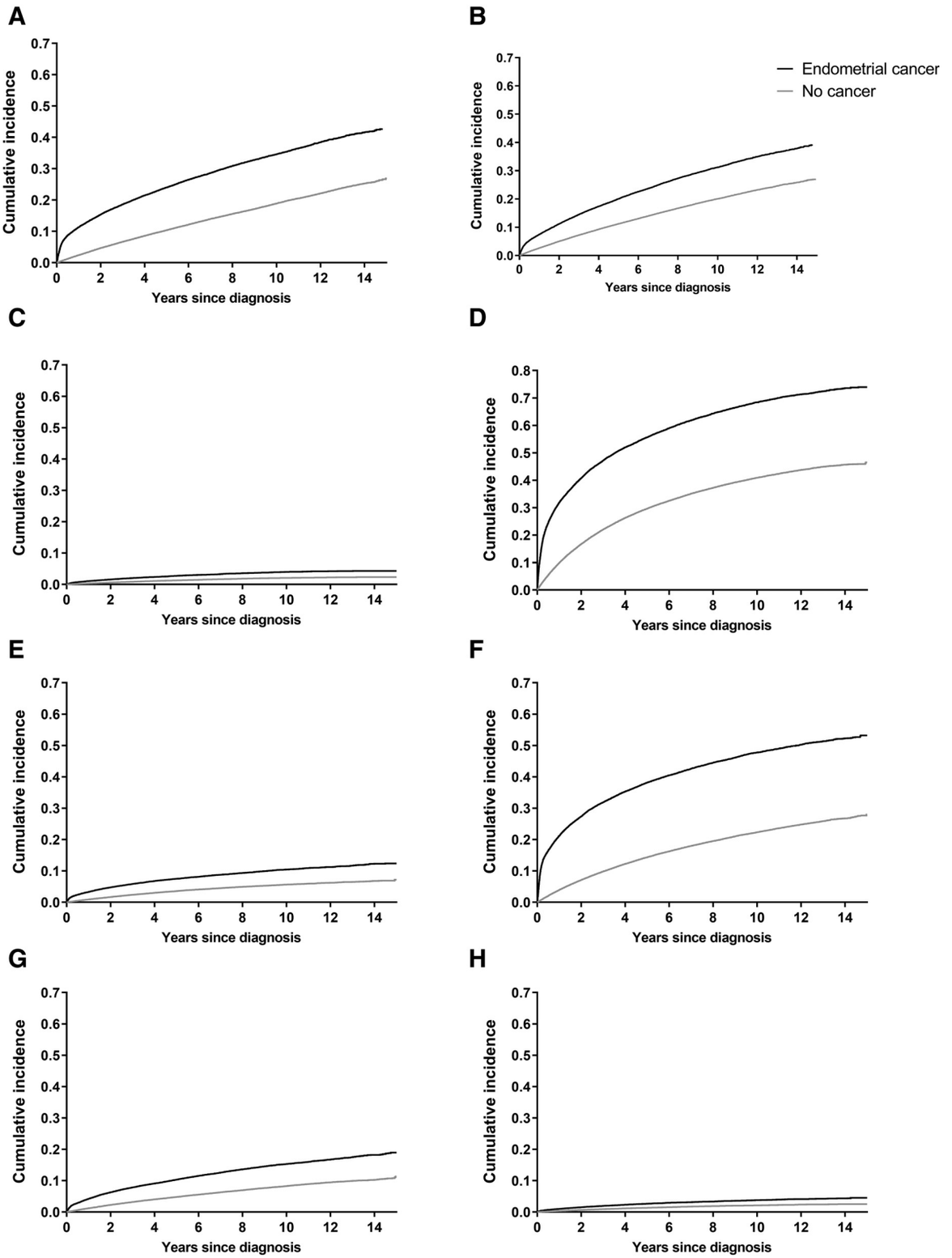

Figure 1.

Cumulative incidence of renal failure (**A**), CKD (**B**), glomerular diseases (**C**), lower UTIs (**D**), calculus of the urinary tract (**E**), other kidney and urinary diseases (**F**), bladder diseases (**G**), and urethra diseases (**H**).

Table 3. Urinary outcomes among older women with endometrial cancer and matched women without cancer.

	Endometrial cancer		No cancer		
	N women	*N* events	*N* women	*N* events	HR (95% CI)[a]
Urinary system diseases					
Renal failure	42,505	11,586	215,366	21,098	2.28 (2.23–2.33)
CKD	40,990	9,703	209,956	22,080	1.85 (1.81–1.90)
Glomerular diseases	43,997	1,316	220,010	2,501	1.94 (1.81–2.07)
Calculus of the urinary tract	43,172	3,545	218,284	6,789	2.22 (2.13–2.31)
Other diseases of the kidney and ureter	39,771	15,854	26,219	26,219	3.06 (3.00–3.12)
Lower UTI	30,884	17,532	186,627	46,791	2.36 (2.32–2.40)
Diseases of the bladder	43,163	5,077	217,577	9,562	2.29 (2.21–2.37)
Diseases of the urethra	43,810	1,270	220,143	2,611	2.06 (1.93–2.21)

[a]Adjusted for age at start of follow-up, race/ethnicity, region, Charlson score.

In analyses starting follow-up at 1 year after endometrial cancer diagnosis, cancer treatment type was also associated with several urinary outcomes (**Table 5**). Women treated with chemotherapy and/or radiation, in addition to hysterectomy, had a higher risk of most urinary outcomes than women treated with hysterectomy alone. HR estimates were generally higher among those who received chemotherapy and hysterectomy (with or without radiation) than among those who received radiation and hysterectomy without chemotherapy. For all study outcomes, HRs were highest for women who received chemotherapy and/or radiation without hysterectomy compared with hysterectomy alone. Estimates were generally attenuated or no longer statistically significant in analyses beginning follow-up at 5 years after endometrial cancer diagnosis (Supplementary Table S4).

Discussion

Using cancer registry data linked to Medicare claims, we examined the risk of urinary diseases among older women with an endometrial cancer history. We found that several urinary outcomes, particularly lower UTIs and kidney-related diseases such as renal failure and CKD, were common after endometrial cancer, with the cumulative incidence of these conditions surpassing 20% by 5 years after cancer diagnosis. For all urinary outcomes that we examined, the risk among endometrial cancer survivors significantly exceeded that among matched women without a cancer diagnosis. In addition to demographic predictors such as age and race/ethnicity, characteristics associated with a higher risk of adverse urinary outcomes among endometrial cancer survivors tended to include higher stage or grade cancer, and receipt of chemotherapy and/or radiation.

Prior studies with a focus on urinary-related outcomes among women with endometrial cancer have generally relied on self-reported to measures to assess urinary symptoms, such as incontinence, leakage, and pain, and have often lacked a comparison group of similarly aged women without a cancer history (5–8). To date, our study is one of few to examine diagnoses of urinary diseases among women with and without endometrial cancer using large-scale, systematically collected national data, though our results do support those of previous investigations. In a report using cancer registry and electronic medical record data in Utah, women with an endometrial cancer diagnosis at ages 18 years or older were at an increased risk of all urinary disease diagnoses, relative to women from the general population, at 1+ years post-cancer diagnosis (HR = 1.50; 95% CI, 1.40–1.62; ref. 15). Although their population was younger, on average, and less geographically and racially diverse than our cohort, their HR estimates for individual urinary conditions such as renal failure, CKD, UTIs, and diseases of the bladder and urethra were generally similar to those of the current study.

Several factors may help to explain the observed differences in risk of urinary diseases between endometrial cancer survivors and cancer-free women. One of these may be a higher prevalence of obesity and obesity-related comorbidities in the endometrial cancer group. Obesity has been associated with a higher risk of developing endometrial cancer (16), and is also a risk factor for some urinary diseases, especially those related to kidney function (i.e., CKD, renal failure; ref. 17). Because body mass index (BMI) is not routinely captured by cancer registry or claims data, we were unable to account for it in our multivariable models. In the Utah study, urinary disease risks were still elevated after endometrial cancer even with additional adjustment for BMI, and BMI was not significantly associated with risk of all urinary diseases combined among survivors (15), suggesting that BMI alone may not fully explain our findings. Nevertheless, it is worth noting that in our cohort, the prevalence of most urinary outcomes in the year prior to the index date was higher among women with endometrial cancer than among matched comparators, indicating that higher BMI and/or other pre-cancer exposures at least partially explain the higher risk of urinary diseases among endometrial cancer survivors.

Our results suggest that treatments for endometrial cancer may also contribute to urinary disease risk. Among older survivors in our study, risk was generally higher for women who received chemotherapy and/or radiation as part of their treatment, compared with those who received hysterectomy alone. Those with chemotherapy seemed to be at particularly elevated risk of several outcomes. This is consistent with findings from the Utah study, where HR estimates for all urinary system disorders within 1 to 5 years post-diagnosis were 1.46 (95% CI, 1.26–1.69) for surgery and radiation, 2.99 (95% CI, 2.21–4.04) for surgery and chemotherapy, and 2.34 (95% CI, 1.81–3.02) for surgery, radiation, and chemotherapy, relative to surgery only (15). These findings may be partially explained by more advanced cancer stages among those treated with chemotherapy and/or radiation, and the difficulty in disaggregating direct effects of these therapies from effects of progression of the cancer itself. However, a number of chemotherapeutic agents can cause nephrotoxicity, and both chemotherapy and pelvic radiation can damage the bladder (18, 19), and these effects could potentially manifest clinically in some of the urinary diagnoses we examined. Taken together, our results and those of prior investigations suggest that monitoring for urinary diseases may be an especially critical part of survivorship care for endometrial cancer patients treated with chemotherapy and/or radiation.

The ability to assess differences according to race/ethnicity is a unique aspect of our analyses, as few other studies of urinary-related

Table 4. Adjusted HRs for associations between demographic and cancer characteristics and urinary outcomes among women with endometrial cancer, with follow-up beginning at endometrial cancer diagnosis.

	Renal failure HR (95% CI)[a]	CKD HR (95% CI)[a]	Glomerular disease HR (95% CI)[a]	Calculus of the urinary tract HR (95% CI)[a]	Other diseases of the kidney/ureter HR (95% CI)[a]	Lower UTI HR (95% CI)[a]	Diseases of the bladder HR (95% CI)[a]	Diseases of the urethra HR (95% CI)[a]
Age at cancer diagnosis								
66–69	1	1	1	1	1	1	1	1
70–74	1.20 (1.13–1.27)	1.22 (1.14–1.30)	1.11 (0.95–1.31)	1.04 (0.94–1.14)	1.12 (1.07–1.18)	1.06 (1.01–1.11)	1.18 (1.09–1.28)	1.17 (0.99–1.38)
75–79	1.47 (1.38–1.56)	1.47 (1.37–1.57)	1.22 (1.02–1.44)	0.93 (0.83–1.03)	1.21 (1.15–1.27)	1.25 (1.19–1.31)	1.27 (1.16–1.39)	1.13 (0.94–1.35)
80–84	1.73 (1.62–1.85)	1.82 (1.69–1.96)	1.00 (0.81–1.23)	0.91 (0.80–1.04)	1.30 (1.22–1.38)	1.42 (1.34–1.50)	1.33 (1.20–1.48)	1.32 (1.08–1.62)
85+	2.05 (1.89–2.21)	2.10 (1.93–2.28)	0.89 (0.68–1.15)	0.74 (0.63–0.88)	1.34 (1.25–1.44)	1.51 (1.42–1.62)	1.27 (1.12–1.45)	1.25 (0.98–1.61)
P_{trend}	<0.001	<0.001	0.689	<0.001	<0.001	<0.001	<0.001	0.024
Race/ethnicity								
White	1	1	1	1	1	1	1	1
Black	1.72 (1.61–1.84)	1.58 (1.46–1.71)	1.56 (1.28–1.89)	0.95 (0.83–1.10)	1.30 (1.22–1.38)	0.99 (0.93–1.05)	0.87 (0.77–0.99)	0.80 (0.61–1.04)
Other	0.93 (0.79–1.11)	0.92 (0.76–1.11)	1.29 (0.85–1.94)	1.15 (0.88–1.49)	1.09 (0.95–1.24)	0.91 (0.80–1.04)	0.78 (0.60–1.01)	1.02 (0.64–1.61)
Asian	0.95 (0.79–1.13)	1.03 (0.86–1.24)	1.10 (0.70, 1.75)	0.82 (0.59–1.15)	1.09 (0.95–1.25)	0.97 (0.84–1.11)	0.90 (0.69–1.16)	0.65 (0.36–1.18)
Hispanic	0.95 (0.78–1.17)	1.03 (0.86–1.24)	1.17 (0.70–1.95)	1.07 (0.76–1.50)	1.03 (0.88–1.22)	1.17 (1.00–1.37)	1.22 (0.94–1.60)	1.03 (0.58–1.83)
North American Native	1.15 (0.71–1.89)	1.24 (0.76–2.03)	0.95 (0.24–3.81)	0.77 (0.29–2.06)	1.45 (1.02–2.06)	0.84 (0.55–1.28)	0.94 (0.45–1.97)	2.15 (0.80–5.75)
Unknown	0.79 (0.47–1.34)	0.94 (0.54–1.61)	NC	1.08 (0.56–2.08)	0.74 (0.51–1.09)	0.81 (0.59–1.12)	1.30 (0.75–2.25)	1.13 (0.36–3.53)
Region								
Midwest	1.16 (1.08–1.25)	1.27 (1.18–1.37)	1.11 (0.90–1.37)	0.96 (0.84–1.09)	1.00 (0.94–1.07)	0.96 (0.91–1.02)	0.95 (0.84–1.06)	0.76 (0.60–0.97)
Northeast	1	1	1	1	1	1	1	1
South	1.18 (1.11–1.26)	1.28 (1.20–1.37)	1.04 (0.86–1.25)	0.97 (0.86–1.08)	0.99 (0.94–1.05)	1.00 (0.95–1.05)	1.13 (1.03–1.24)	1.01 (0.84–1.22)
West	0.93 (0.88–0.98)	1.09 (1.03–1.15)	1.01 (0.87–1.17)	0.90 (0.82–0.98)	0.95 (0.91–0.99)	1.00 (0.96–1.04)	1.03 (0.95–1.11)	1.02 (0.89–1.18)
Charlson score								
0	1	1	1	1	1	1	1	1
1	1.38 (1.31–1.46)	1.43 (1.35–1.52)	2.34 (1.94–2.83)	1.17 (1.06–1.29)	1.12 (1.07–1.17)	1.21 (1.16–1.27)	1.09 (1.01–1.18)	1.13 (0.97–1.32)
2+	2.38 (2.26–2.50)	2.25 (2.13–2.38)	4.92 (4.16–5.81)	1.62 (1.48–1.76)	1.54 (1.48–1.61)	1.51 (1.45–1.58)	1.38 (1.29–1.49)	1.28 (1.11–1.48)
P_{trend}	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Stage								
Local	1	1	1	1	1	1	1	1
Regional	1.43 (1.36–1.50)	1.34 (1.27–1.42)	1.29 (1.11–1.49)	1.24 (1.13–1.35)	1.45 (1.39–1.51)	1.23 (1.18–1.28)	1.28 (1.19–1.38)	1.09 (0.93–1.27)
Distant	3.36 (3.12–3.62)	2.30 (2.09–2.53)	1.89 (1.46–2.45)	1.85 (1.59–2.16)	2.35 (2.20–2.51)	1.91 (1.79–2.04)	1.77 (1.54–2.02)	1.50 (1.13–1.99)
Histology								
Endometrioid	1	1	1	1	1	1	1	1
Serous	0.98 (0.90–1.06)	1.06 (0.97–1.17)	0.71 (0.54–0.94)	1.30 (1.12–1.51)	1.12 (1.05–1.20)	1.00 (0.93–1.07)	1.06 (0.93–1.21)	1.19 (0.92–1.55)
Carcinosarcoma	1.32 (1.21–1.45)	1.25 (1.12–1.40)	1.23 (0.93–1.63)	1.53 (1.28–1.82)	1.40 (1.29–1.51)	1.08 (0.99–1.17)	1.02 (0.86–1.21)	1.39 (1.02–1.91)
Clear Cell	1.04 (0.89–1.20)	1.15 (0.97–1.36)	0.88 (0.55–1.41)	0.70 (0.50–0.99)	1.01 (0.89–1.15)	0.94 (0.82–1.07)	1.01 (0.79–1.29)	1.50 (0.98–2.30)
Mixed	1.04 (0.96–1.13)	1.04 (0.94–1.14)	0.88 (0.68–1.13)	0.97 (0.83–1.14)	1.01 (0.94–1.08)	1.01 (0.95–1.09)	1.14 (1.01–1.29)	0.86 (0.65–1.13)
Other	1.37 (1.22–1.54)	1.20 (1.04–1.38)	0.76 (0.50–1.17)	1.09 (0.86–1.39)	1.55 (1.41–1.71)	1.26 (1.14–1.40)	1.36 (1.13–1.63)	1.00 (0.65–1.53)
Grade								
1	1	1	1	1	1	1	1	1
2	1.09 (1.03–1.15)	1.07 (1.01–1.13)	0.93 (0.80–1.08)	1.07 (0.98–1.18)	1.15 (1.10–1.21)	1.10 (1.06–1.15)	1.06 (0.98–1.15)	1.19 (1.03–1.39)
3	1.34 (1.26–1.43)	1.14 (1.07–1.22)	1.09 (0.92–1.31)	1.08 (0.96–1.21)	1.34 (1.27–1.41)	1.17 (1.11–1.23)	1.08 (0.99–1.19)	1.12 (0.93–1.36)
Undifferentiated	1.40 (1.28–1.52)	1.10 (1.00–1.22)	1.21 (0.93–1.58)	1.12 (0.95–1.32)	1.39 (1.29–1.49)	1.16 (1.08–1.25)	1.15 (1.00–1.31)	1.01 (0.76–1.35)

[a]Adjusted for age at cancer diagnosis, race/ethnicity, region, Charlson score, stage, histology, grade.

Table 5. Associations between cancer treatment and urinary outcomes among women with endometrial cancer, with follow-up beginning at 1 year after endometrial cancer diagnosis.

	Renal failure HR (95% CI)[a]	CKD HR (95% CI)[a]	Glomerular disease HR (95% CI)[a]	Calculus of the urinary tract HR (95% CI)[a]	Other diseases of the kidney/ureter HR (95% CI)[a]	Lower UTI HR (95% CI)[a]	Diseases of the bladder HR (95% CI)[a]	Diseases of the urethra HR (95% CI)[a]
Treatment								
Hysterectomy only	1	1	1	1	1	1	1	1
Hysterectomy + radiation	1.13 (1.05–1.21)	1.05 (0.99–1.13)	1.07 (0.88–1.29)	1.21 (1.08–1.36)	1.08 (1.02–1.15)	1.06 (1.01–1.12)	1.20 (1.09–1.31)	1.32 (1.10–1.58)
Hysterectomy + chemotherapy	1.38 (1.23–1.54)	1.14 (1.01–1.28)	1.22 (0.88–1.69)	1.16 (0.94–1.43)	1.24 (1.12–1.38)	1.13 (1.03–1.25)	1.27 (1.07–1.50)	0.99 (0.69–1.41)
Hysterectomy + radiation + chemotherapy	1.24 (1.12–1.36)	1.19 (1.08–1.31)	1.28 (0.97–1.67)	1.24 (1.05–1.47)	1.23 (1.13–1.35)	1.04 (0.96–1.13)	1.52 (1.33–1.74)	1.24 (0.95–1.63)
Chemotherapy and/or radiation	2.14 (1.86–2.47)	1.48 (1.24–1.75)	2.49 (1.73–3.58)	1.35 (0.98–1.84)	1.60 (1.38–1.85)	1.66 (1.44–1.90)	1.85 (1.47–2.32)	1.40 (0.84–2.31)

[a]Adjusted for age at cancer diagnosis, race/ethnicity, region, Charlson score, stage, histology, grade.

outcomes among endometrial cancer survivors have had sufficient sample size and diversity to investigate these associations. We found that several urinary diseases were more commonly diagnosed among endometrial cancer survivors who were Black, Hispanic, or Asian compared with those who were White. Black survivors were at especially elevated risk of kidney-related conditions (i.e., CKD, renal failure), associations which have been well documented in the general U.S. population, and may be attributable to a number of biological and socioeconomic factors (20–22). Our findings suggest that, in the endometrial cancer context, Black women may be a priority group to target with increased surveillance for urinary conditions during cancer treatment and long-term survivorship.

Our study is among the first and the largest to examine urinary disease diagnoses among older women with endometrial cancer. Use of the SEER-Medicare data allowed us to compare with cancer-free women and to conduct extensive analyses of risks according to demographic and cancer-related characteristics. However, there are some limitations to our analyses. Because BMI is not available in the SEER-Medicare data, we were unable to account for effects of obesity beyond those captured by obesity-related conditions (e.g., diabetes) included in the Charlson comorbidity index. Cancer recurrence is also not reliably identifiable in claims data, so we were unable to assess the role of recurrent disease in our findings. HR estimates from our analyses among women with endometrial cancer were adjusted for summary stage, but residual confounding by more detailed staging criteria may be possible. Because we used diagnosis codes in Medicare claims to define our outcomes, urinary diseases that were undiagnosed/untreated would not be captured by our data. Our analyses also focused on incident urinary diagnoses and did not address potential exacerbation of recurring urinary conditions. Mapping between ICD-9 and ICD-10 diagnosis codes may not be exact, and code lists used for defining our study outcomes have not been previously validated. In addition, diagnosis codes for urinary diseases were required to appear on only one claim to meet our outcome definitions. This could result in overestimation of urinary disease incidence if identified codes reflected 'rule-out' diagnoses rather than actual diagnosed conditions (14).

Results of the current study suggest that older women with endometrial cancer have a higher risk of several urinary outcomes than similarly aged women without a cancer history. Timely identification and treatment of these conditions, especially among those with preexisting risk factors and those treated with chemotherapy and/or radiation, may be an important part of ongoing survivorship care after endometrial cancer.

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J.L. Lund reports grants from Roche; and grants from AbbVie outside the submitted work; and Dr. Lund's spouse was formerly employed by GlaxoSmithKline and previously owned stock in the company. No disclosures were reported by the other authors.

Authors' Contributions

C. Anderson: Conceptualization, formal analysis, writing–original draft, writing–review and editing. **A.F. Olshan:** Writing–review and editing. **J. Park:** Writing–review and editing. **V.L. Bae-Jump:** Writing–review and editing. **W.R. Brewster:** Writing–review and editing. **J.L. Lund:** Writing–review and editing. **H.B. Nichols:** Supervision, writing–review and editing.

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