

Long Term Kidney Outcomes in Wilms Tumor Survivors

Shannon Reinert, MD¹; Rajaram Nagarajan, MD, MS^{2,3}; Stefanie Benoit, MD, MPH^{3,4}



¹Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA; ²Division of Oncology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA; ³Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA; ⁴Division of Nephrology and Hypertension, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA.

Background

- Wilms Tumor (WT) is the most common pediatric kidney tumor.
- With improved survival rates over the past few decades, long term adverse effects of WT treatment have become more important to understand.
- Potential adverse kidney outcomes in WT survivors include decreased glomerular filtration rate (GFR), proteinuria, lack of compensatory hypertrophy (CH) in the contralateral kidney, and hypertension (HTN).
- Existing studies evaluating for long term kidney dysfunction in WT survivors have small sample sizes and report a wide variability in the risk of long-term kidney dysfunction.
- Many studies exclude patients at highest risk for poor kidney outcomes, including only those with unilateral, non-syndromic WT. Some even exclude patients who received nephrotoxic chemotherapy or radiation.

Objective

To investigate long-term kidney outcomes of WT survivors at Cincinnati Children's Hospital Medical Center, including high risk survivors and using updated GFR estimation equations.

Methods

Study Design

- Retrospective chart review of patients treated for WT at CCHMC who were diagnosed from 3/1/2000-2/1/2016, ≥ 5 years off therapy, and in remission.
- Excluded patients with missing data.
- Charts were reviewed for evidence of decreased eGFR, hypertension, proteinuria, and compensatory hypertrophy (CH) of the contralateral kidney.
- GFR was estimated using (1) serum creatinine only (sCr) and (2) cystatin C (CysC) + sCr combined CKID U25 equations

Statistical Methods

- Chi-squared tests and t-tests were used to test for significant associations.

Results

Demographic and Clinical Characteristics of Wilms Tumor Patients	
Total Subjects (M/F)	49 (22/27)
Median age at diagnosis in years (IQR)	3 (1.58-4.83; range 0-8.58)
Race, n (%)	White 40 (82%) Black 6 (12%) Other 1 (2%) Unknown 2 (4%)
Ethnicity, n (%)	Non-Hispanic 46 (94%) Hispanic 2 (4%) Unknown 1 (2%)
WT Stage at Diagnosis, n (%)	Stage 1 7 (14%) Stage 2 16 (33%) Stage 3 14 (29%) Stage 4 8 (16%) Stage 5 4 (8%)
Tumor Localization, n (%)	Left 26 (53%) Right 19 (39%) Bilateral 4 (8%)
Relapse, n (%)	3/49 (6%)
Type of Nephrectomy, n (%)	Radical 47 (96%) Partial 2 (4%)
Type of Chemotherapy, n (%)	Vincristine 49 (100%) Dactinomycin 48 (98%) Doxorubicin 27 (55%) Cyclophosphamide 9 (18%) Etoposide 9 (18%) Carboplatin 3 (6%)
Radiation, n (%)	23/49 (47%)
Radiation to remaining kidney, n (%)	9/49 (18%)
Blood Pressure Follow up time in years, n (%)	5-9 14 (29%) 10-14 19 (39%) 15-20 16 (33%)
eGFR Follow up time in years, n (%)	5-9 20 (41%) 10-14 16 (33%) 15-20 13 (27%)

The Effect of Whole Abdominal Radiation on Kidney Outcomes			
	Whole Abdominal Radiation	No Abdominal Radiation	P-value
Most Recent Blood Pressure			
Normal	5 (56%)	22 (55%)	0.113
Elevated	1 (11%)	14 (35%)	
Hypertension	3 (33%)	4 (10%)	
Compensatory Hypertrophy			
Yes	5 (56%)	23 (64%)	0.711
No	4 (44%)	13 (36%)	
Median eGFR (IQR)			
U25-sCr only	95 (73-105)	95 (86-105)	0.339
U25-sCr + CysC	80 (65-94)	93 (85-99)	0.140

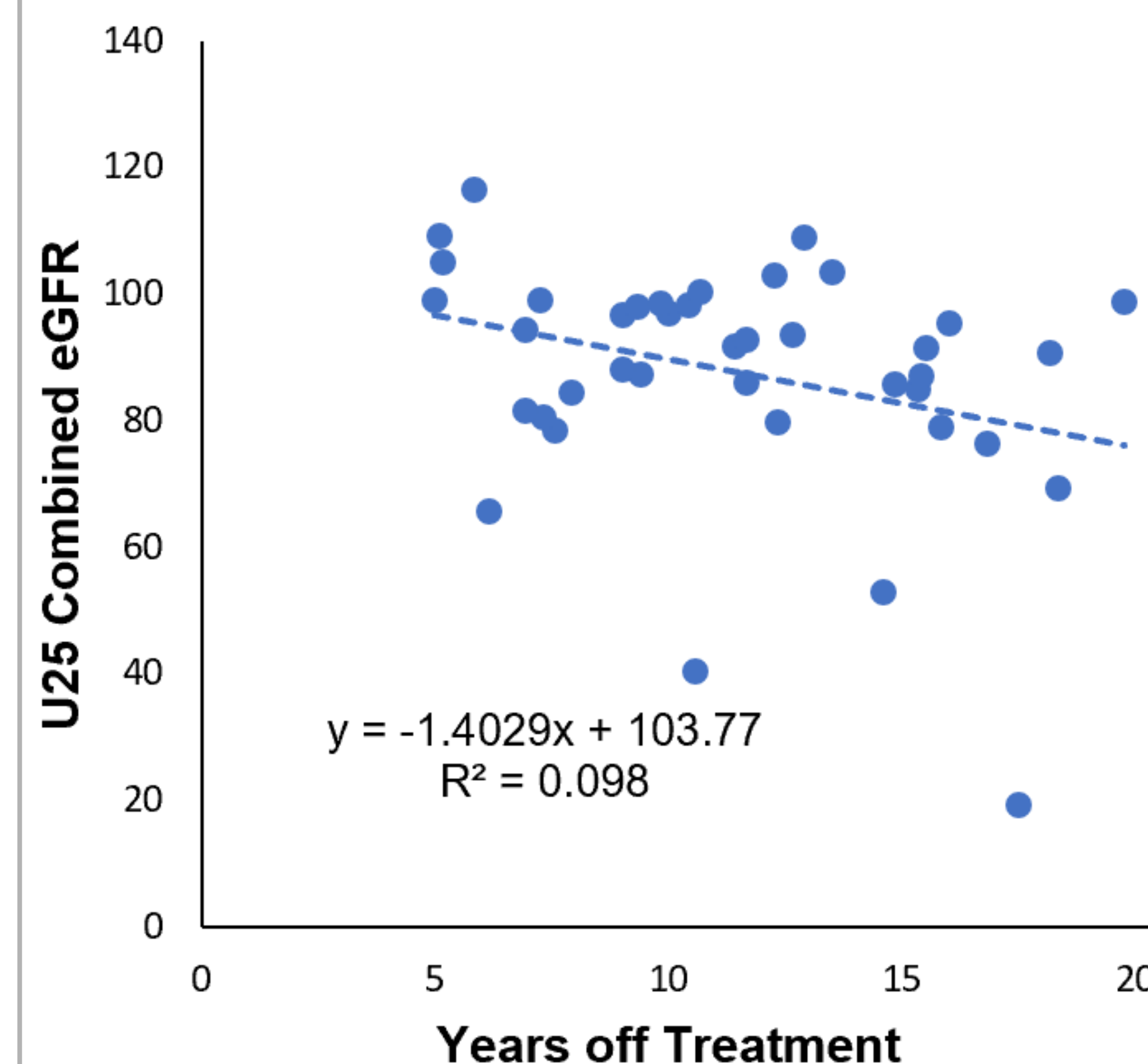
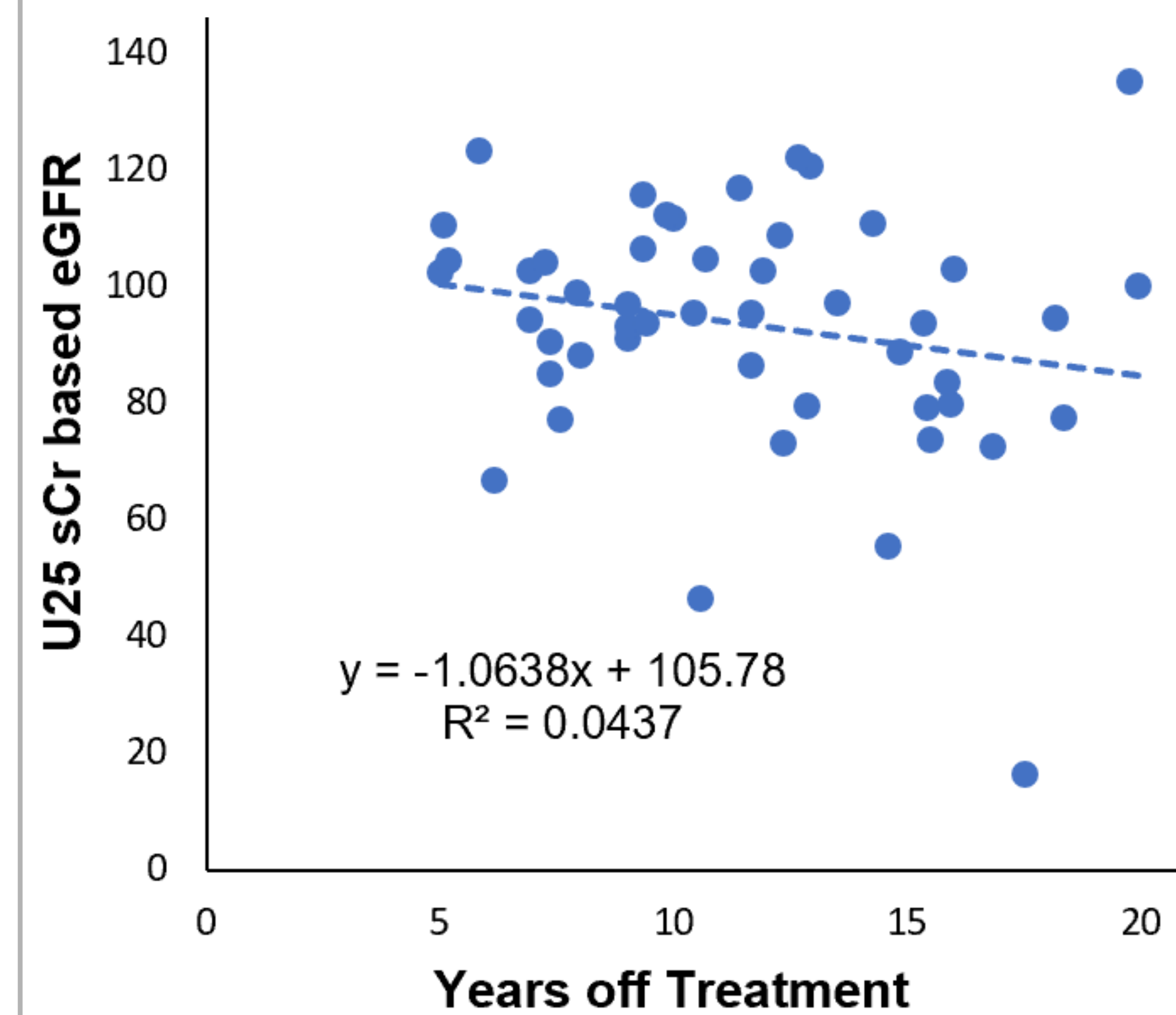
Effect of Age at Diagnosis on Kidney Outcomes			
	0-35 Months at Diagnosis	≥36 Months at Diagnosis	P-value
Most Recent Blood Pressure			
Normal	11 (46%)	16 (64%)	0.054
Elevated	11 (46%)	4 (16%)	
Hypertension	2 (8%)	5 (20%)	
Compensatory Hypertrophy			
Yes	16 (73%)	12 (52%)	0.221
No	6 (27%)	11 (48%)	
eGFR (Creatinine only)			
≥90	15 (63%)	17 (68%)	0.724
60-90	8 (33%)	6 (24%)	
<60	1 (4%)	2 (8%)	

- There was no relationship between whole abdominal radiation and eGFR, blood pressure, or presence of compensatory hypertrophy.
- There was no relationship between age at diagnosis and eGFR, blood pressure, or presence of compensatory hypertrophy.

Results

eGFR at most recent follow up			
eGFR (mL/min/1.73 m ²)	>90	60-90	<60
Creatinine only	32 (65%)	14 (29%)	3 (6%)
Creatinine + CysC	22 (55%)	15 (38%)	3 (8%)

eGFR trend with increasing follow up intervals



- A significant number of patients had evidence of decreased GFR.
- A decreasing trend in eGFR was seen with increased follow up time, similar to prior studies.
- One patient had ESRD s/p kidney transplant.

Results

Blood Pressure at Most Recent Visit	
Normal	27 (55%)
Elevated	15 (31%)
Stage 1 Hypertension	6 (12%)
Stage 2 Hypertension	1 (2%)

Presence of Compensatory Hypertrophy (Kidney Length >2 SD above mean kidney length based on height)	
Yes	28 of 45 with unilateral nephrectomy (62%)
Median eGFR with CH (IQR)	95 (83-106) ml/min/1.73m ²
Median eGFR without CH (IQR)	95 (87-103) ml/min/1.73m ²

Proteinuria (Urine protein-to-creatinine ratio > 0.2 mg/mg)	
Yes	8 of 27 (30%)
Persistent proteinuria	3 of 6 (50%)

Outcomes for Hispanic and Black patients			
Race/Ethnicity		Hispanic or Black	Non-Hispanic White
Stage at Diagnosis	I	0	7 (17.5%)
	II	1 (13%)	15 (37.5%)
	III	3 (38%)	10 (25%)
	IV	3 (38%)	5 (12.5%)
	V	1 (13%)	3 (7.5%)
Compensatory Hypertrophy	Yes	4 (50%)	24 (61.5%)
	No	4 (50%)	15 (38.5%)
Proteinuria	Yes	3 (60%)	5 (22.7%)
	No	2 (40%)	17 (77.3%)
eGFR (sCr Only)	≥90	4 (50%)	27 (67.5%)
	60-90	2 (25%)	12 (30%)
	<60	2 (25%)	1 (2.5%)
Most Recent Blood Pressure	Normal	3 (43%)	23 (57.5%)
	Elevated	3 (43%)	12 (30%)
	Stage 1 HTN	2 (29%)	4 (10%)
	Stage 2 HTN	0	1 (2.5%)

- Black and Hispanic children in our study tended to present at a later stage and appeared to have worse long-term kidney outcomes.
- Small sample size precludes statistical analysis of differences in the outcomes of racial/ethnic minorities.

Conclusions

- Kidney dysfunction is common in survivors of WT. This population should be monitored carefully for the development of decreased GFR, hypertension, and proteinuria.
- Larger, multi-centered studies are needed to assess the effect of nephrotoxic chemotherapy, whole abdominal radiation, and age at diagnosis on long term kidney outcomes.
- Additional studies are needed to assess the impact of racial/ethnic and socioeconomic factors on kidney outcomes in WT survivors.