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Diagnosis of renal tumors in Birt-Hogg-Dube syndrome: Clinical presentation and risk factors in a single-center retrospective cohort

Supiya Kijlertsuphasri[1,2], Tananchai Petnak[2] and Teng Moua[1*]

Abstract

Background Birt-Hogg-Dube (BHD) syndrome is a rare genetic condition associated with the development of renal tumors. This study aims to determine typical age ranges for detecting renal abnormalities, risk factors for tumor development, and long-term outcomes based on current surveillance strategies.

Methods A single-center multi-site retrospective cohort study was performed on all patients with BHD diagnosed from 2000 to 2023. Baseline demographics, pulmonary function, laboratory, radiologic, and histopathologic findings were collected. Logistic regression was used to assess predictor variables for the development of renal tumors with survival analysis evaluated from the date of BHD diagnosis to date of death or last known follow-up.

Results The study included 149 patients with BHD, 39 (26%) with diagnosed renal tumors, of which 28 had histopathologic confirmation. Mean age at renal tumor detection was 53.61 years. Older age and male sex were predictive of renal tumor development ((odds ratio 1.05; 95% CI, 1.01–1.08, $P=0.002$) and (odds ratio 2.59; 95% CI, 1.17–5.73, $P=0.02$), respectively). Time to all-cause mortality appeared shorter in those with renal tumors (Log-rank $P=0.02$), though no deaths were from cancer or cancer-related complications.

Conclusions Current screening protocols for renal tumors in BHD suggest the most common presenting age range for presentation is late 40s to early 50s, with older age and male sex as risk factors for tumor development.

Keywords Birt-Hogg-Dube, Renal tumor, Renal carcinoma, Cystic lung disease, Cancer screening

Background

Birt-Hogg-Dube´(BHD) syndrome is a rare autosomal dominant disease caused by germline mutations in the folliculin (*FLCN*) gene on chromosome 17 [1]. Common clinical manifestations include pulmonary cysts [2], dermal fibrofolliculomas [3], and renal tumors [4]. Multiple chromophobe renal cell carcinoma and hybrid oncocytic tumor are the most common renal tumor subtypes in BHD and a leading cause of morbidity [5]. However, there is limited understanding of specific risk factors for the development of renal tumors in BHD and recommendations for surveillance or follow-up.

Experts have previously suggested screening for renal tumors at the age of 20 with annual abdominal magnetic resonance imaging (MRI) scans [6]. Prior recommendations have suggested imaging every three years in those with initially normal findings [7], while a most recent guideline suggested imaging every 1–2 years [8]. Detected renal tumors smaller than 3 centimeters may

*Correspondence:
Teng Moua
moua.teng@mayo.edu
[1]Division of Pulmonary and Critical Care Medicine, Mayo Clinic, 200 First St SW, 55905 Rochester, MN, USA
[2]Division of Pulmonary and Pulmonary Critical Care Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Salaya, Thailand

be followed, while surgical excision is recommended for those larger than 3 centimeters [6, 7]. Few studies have specifically reviewed the screening or diagnosis of renal tumors in BHD [5, 6], with current practices primarily adapted from those used in other hereditary renal cell carcinomas [9].

Our study aims to assess in a real-world BHD population common ages for renal tumor presentation at baseline or on surveillance imaging, risk factors for their development, and optimal strategies for follow-up or monitoring in those with initially normal imaging or smaller unresected tumors.

Methods

Study design

Institutional review board approval was completed before study initiation (Mayo Clinic IRB 23-012463). The study design is a retrospective cohort involving patients seen and followed at all Mayo Clinic sites (Minnesota, Florida, and Arizona) between 2000 and 2023 with BHD syndrome. A computer-assisted search of the electronic medical record (EMR) was performed using related ICD9 and ICD-10-CM diagnosis codes for *'other specified congenital malformation syndromes'* and *'Birt Hogg Dube'* as a text search in clinical notes and test reports. Individual patient records were reviewed for BHD diagnosis according to diagnostic criteria presented by Menko et al. [6] This included patients with one major or two minor criteria as below:

Major criteria

- At least five fibrofolliculomas or trichodiscomas, with one histologically confirmed, of adult onset.
- Pathogenic *FLCN* germline mutation.

Minor criteria

- Multiple lung cysts: bilateral basally located lung cysts with no other apparent cause, with or without spontaneous primary pneumothorax.
- Renal cancer: early onset (< 50 years) or multifocal or bilateral renal cancer, or renal cancer of mixed chromophobe and oncocytic histology.
- A first-degree relative with BHD.

Data collection

Baseline demographics, radiologic, and laboratory findings were collected from the EMR for each included case. Age at BHD diagnosis and the first detection of renal abnormalities on imaging, sex, smoking history, *FLCN* gene mutation status, renal function, and urinalysis in those with tumor diagnosis, the first occurrence of BHD-related clinical signs or symptoms, and presence of dermatologic, pulmonary cystic, and pneumothorax were collated. Collated lung function included percent predicted forced vital capacity (FVC%), forced expiratory volume in the first second (FEV1%), and diffusion capacity for carbon monoxide (DLCO%). Data regarding renal tumors included initial and longitudinal changes in size on imaging, histopathology, staging, directed treatments, and long-term outcomes. Lung cysts were confirmed and followed with chest computed tomography (CT); dermatological findings were confirmed on dermal biopsy as fibrofolliculoma or trichodiscoma, and renal tumors were detected or identified with either abdominal CT or magnetic resonance imaging (MRI).

Data analysis

Continuous data with normal distributions were presented as mean and standard deviation (SD). Categorical data were presented as frequencies and percentages. Baseline characteristics among patients with or without renal tumors were compared using t-test for continuous variables and Chi-square or Fisher's exact test for categorical variables. Predictor variables for the development of renal malignancy were assessed using univariable and multivariable logistic regression, adjusted for a priori covariables of age at BHD diagnosis, sex, and smoking history. Odds ratios (OR) or point estimates were provided with 95% confidence intervals. Survival analysis was assessed from the date of BHD diagnosis to the date of death or last known follow-up using Log-rank with Kaplan-Meier, stratified by the presence of renal malignancy. Two-tailed P values < 0.05 were considered statistically significant. All statistical analysis was completed with BlueSky Statistics software v. 10.3 (BlueSky Statistics LLC, Chicago, IL, USA).

Results

Study screening and enrollment are presented in Fig. 1. A search of the EMR from January 2000 to October 2023 using ICD code Q87.89 ('other congenital malformation syndromes') and search term *'birt hogg dube'* identified 189 potential cases. Individual records were reviewed, with 149 meeting one major or two minor diagnostic criteria for BHD syndrome [6].

Baseline characteristics in patients with ($n=39$) and without renal tumor ($n=110$) are presented in Table 1. Those with renal tumor were older at the time of BHD diagnosis (56 vs. 46.7, $P=0.002$), male (64% vs. 41%, $P=0.01$), had greater smoking history (44% vs. 24%, $P=0.02$), lower FEV1% at presentation (82.7% vs. 93.8%, $P=0.02$), and increased dermatological findings (46% vs. 27%, $P=0.04$). Incidental renal tumors seen on imaging as a first clinical sign of BHD occurred in 20 of 39

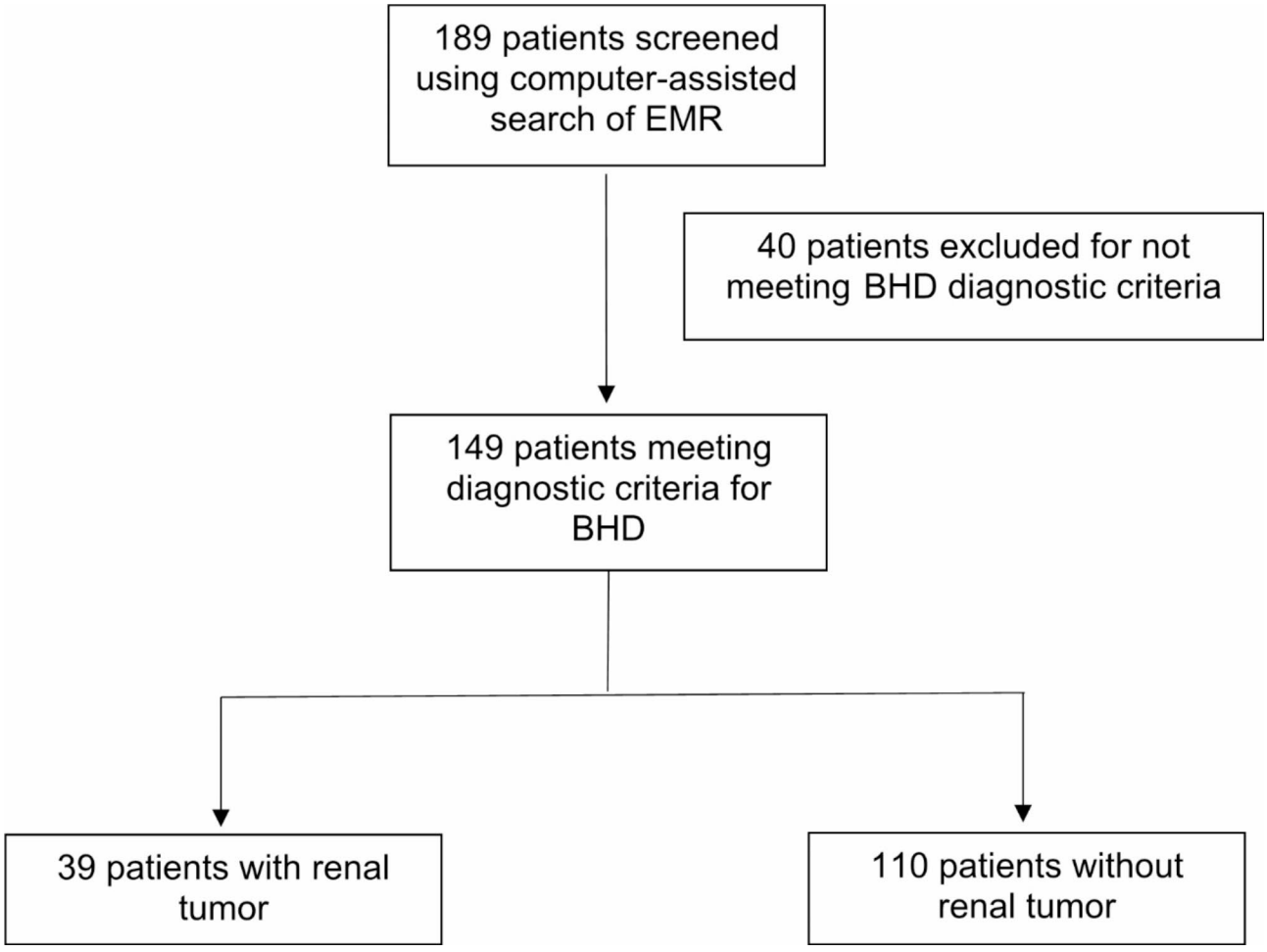

Fig. 1 Study screening and inclusion. BHD = Birt-Hogg-Dube´

patients (51%), while fibrofolliculoma (62%), pneumothorax (32%), and family history (32%) were common initial clinical findings in those without subsequent tumor. As initial tumor findings on imaging often pre-dated formal BHD diagnosis, mean age at tumor detection was 53.6 years. Forty-five unique tumors were diagnosed among 39 patients (10 patients had more than one tumor per kidney), with a median size of 2 cm (range 0.5 to 12 cm) at first radiologic detection. Microscopic hematuria was observed in four patients (21% of tested patients) at the time of tumor diagnosis.

Characteristics, staging, and management of renal cancer in 28 patients with pathologically confirmed disease are presented in Table 2. Among these, 16 patients were found to have renal tumors larger than 3 cm, six less than 3 cm, and six without data on tumor size at the time of resection. Twenty-six had urological procedures at the time of initial radiologic presentation. Only two had renal tumors measuring initially 0.5 centimeters and 3 centimeters, followed for 4 and 2 years, respectively. They were later measured at 1.8 centimeters and 4 centimeters, respectively. One was followed with a yearly MRI noting renal tumor size increase ranging between 0.1 and 0.3 centimeters per year.

Clear-cell renal cell carcinoma was the most common histopathologic subtype (54%) on biopsy or resection. Of these 15 cases, ten were tested for *FLCN* gene mutation and positive in all ten, with the remainder diagnosed with BHD by clinical criteria. Three patients had other histology including papillary cell carcinoma, low-grade BHD-associated renal cell neoplasm, and mucinous tubular and spindle cell carcinoma. Stage 1 (pT1NanyM0) cancer was present in the majority (79%) at diagnosis. Nephrectomy was the most common treatment approach (79%). One patient, who initially underwent partial nephrectomy for papillary cell-type renal cell carcinoma experienced recurrence at the same site and required additional surgical resection, radiation, and pazopanib-targeted therapy. Another patient was diagnosed with oncocytoma on biopsy and is being followed with annual imaging. All remaining treated patients are currently undergoing follow-up imaging with no signs of tumor recurrence.

Table 1 Baseline characteristics

	BHD with renal tumor (*n* = 39)	BHD without renal tumor (*n* = 110)	*P*-value
Age at diagnosis of BHD, mean (SD)	56.0 (± 15.2)	46.7 (± 15.9)	**0.002**
Age at diagnosis of renal tumor, mean (SD)	53.6 (±12.8)	-	-
Sex			
Male, %	25 (64%)	45 (41%)	**0.01**
Smoking			
Active/prior, %	17 (44%)	25 (24%)	**0.02**
Pack-year, mean (SD)	11 (± 19)	3 (± 9)	**0.001**
Pulmonary function tests at time of BHD diagnosis			
FVC%, mean (SD)	89.6 (± 18.2)	97.0 (± 15.4)	0.12
FEV1%, mean (SD)	82.7 (± 19.9)	93.8 (± 13.6)	**0.02**
DLCO%, mean (SD)	83.6 (± 18.2)	90.5 (± 17.4)	0.20
FLCN gene mutation, %			
FLCN positive	27⁇(90%)	98∴(95%)	0.38
Positive family history of renal cancer, %	7 (18%)	27 (26%)	0.51
Presence of dermatological findings, %	18 (46%)	29 (27%)	**0.04**
Presence of lung cyst, %	23 (59%)	74 (69%)	0.32
Presence of pneumothorax, %	19 (83%)	44 (57%)	**0.03**
Occurrence of first sign or symptom, %			
Lung cysts	1 (2.6%)	12 (11%)	0.11
Pneumothorax	7 (18%)	35 (32%)	0.09
Fibrofolliculoma, Trichodiscoma	18 (38%)	29 (62%)	**0.04**
Occurrence of renal tumor	23 (59%)	-	-
Incidental finding of renal tumor	20	-	
Others			
Hematuria	2	-	
UTI	1		
Family history of FLCN gene abnormality	0 (0%)	35 (32%)	-
Others			
Parotid mass	0 (0%)	1 (0.9%)	-
Urinalysis at diagnosis of renal tumor (*N* = 19)			
Microscopic hematuria, %	4 (21%)	-	-
Creatinine at diagnosis of renal tumor, mean (SD)	0.92 (±0.19)	-	-
Imaging modality for detecting initial renal tumor			
Abdominal Computed Tomography	25 (64%)	-	
Abdominal Magnetic Resonance Imaging	14 (36%)	-	
Tumor size at initial radiologic detection (*N* = 45), cm (median, (range))	2 (0.5–12)		

†: Assessed in 30 cases., ∴: Assessed in 104 cases

BHD = Birt-Hogg-Dube´, SD = standard deviation, BMI = Body mass index, FVC = Forced vital capacity, FEV1 = Forced expiratory volume in the first second, DLCO = diffusing capacity of the lungs for carbon monoxide, FLCN = Folliculin gene, UTI = Urinary tract infection

Eleven of the 39 BHD patients with renal tumors had lesions still measuring less than 3 centimeters and are currently under surveillance. The shortest duration of follow-up was one year, with the longest being 24 years. The maximum growth rate of renal tumors among this group was 0.23 centimeters per year.

Univariable and multivariable logistic regression models assessing risk factors for the development of renal tumors are presented in Table 3. Age at BHD diagnosis (OR 1.04 (1.01–1.07), *P* = 0.003), male sex (OR 2.58 (1.21–5.50), *P* = 0.01), smoking history (OR 2.6 (1.19–5.63), *P* = 0.02), presence of fibrofolliculomas (OR 2.33 (1.09–4.99), *P* = 0.03), presence of pneumothorax (OR 3.56 (1.10-11.46), *P* = 0.03), and lower baseline %FEV1 (OR 0.95 (0.91-1.0), *P* = 0.02) were predictive of renal tumor development on univariable analysis. After adjustment for a priori covariables (age at BHD diagnosis, sex, and smoking history), only age and male sex were predictive (OR 1.05 (1.01–1.08, *P* = 0.002) and 2.59 (1.17–5.73, *P* = 0.02), respectively).

Kaplan-Meier survival analysis is presented in Fig. 2, stratified by the presence of renal tumor. Log-rank testing suggested decreased time to all-cause mortality in those with renal tumors (*P* = 0.02). There were five observed deaths in the tumor group, none of whom died from documented renal cancer, and two in the non-tumor group. Causes of death included pneumonia, acute respiratory

Table 2 Histopathology, staging, and treatment of BHD with renal malignancy

	BHD with renal cancer (*n* = 28)
Age at diagnosis	53.57 (± 11.98)
Method of surveillance	
CT abdomen	19 (73.08%)
MRI abdomen	7 (26.92%)
FLCN gene mutation	18 (64.3%)
Smoking history	11 (39.29%)
Loss follow up	3 (10.71%)
Median size cancer at diagnosis	2.85 (± 1.75)
Skin manifestation	
Fibrofolliculoma, Trichodiscoma	14 (50%)
Lung manifestation	
Lung cysts	19 (67.86%)
Pneumothorax	15 (78.95%)
Pathology, N (%)	
Clear-cell RCC	15 (54%)
Oncocytic/hybrid neoplasm or chromophobe RCC	9 (32%)
Others	3 (11%)
Indeterminate	1 (3%)
TNM stage (pathological), N (%)	
pT1NanyM0	22 (79%)
pT2NanyM0	3 (11%)
pT3NanyM0	1 (3.6%)
pT4NanyM0	1 (3.6%)
pT unknown	1 (3.6%)
Treatment, N (%)	
Nephrectomy	22 (79%)
Radical nephrectomy	21 (95.45%)
Partial nephrectomy	1 (4.55%)
Cryoablation	4 (14%)
Other	2 (7%)

BHD = Birt-Hogg-Dube´, RCC = Renal cell carcinoma

failure, acute renal failure, and septic shock in four, and was unspecified in the remainder.

Most patients with renal tumors in our cohort were diagnosed with BHD after tumors were already present on radiologic assessment. This was often the initial radiologic abnormality prompting workup leading to BHD diagnosis. Only two patients in our cohort were diagnosed with BHD before the development of renal tumors. Patient 1 was diagnosed with BHD in April of 2012 at the age of 55. An initial screening MRI conducted in August of 2016 was unremarkable. A second MRI in November of 2019, a little over three years later, detected a renal mass measuring 3.5 centimeters. Nephrectomy was pursued and confirmed clear cell renal cell carcinoma on histopathology. Patient 2 was diagnosed with BHD in June of 2018 at the age of 47. After initial annual MRI screening studies, a renal tumor was identified on abdominal CT approximately two and a half years later, in December 2020, measuring 1.5 centimeters. MRI of the abdomen in April of 2020, eight months earlier, revealed no abnormalities. A Follow-up MRI in October of 2022 showed an increase to 1.8 centimeters, with the patient continuing observation based on the last available follow-up.

Discussion

Birt-Hogg-Dubé syndrome is a rare autosomal dominant disorder that predisposes affected individuals to developing renal tumors at higher rates than the general population. Our study of 149 patients with BHD assessed the timing of BHD diagnoses and renal tumors, baseline predictors of tumor development, and long-term outcomes. We found most patients in our cohort were not diagnosed with BHD at the time of renal tumor detection, with 51% having renal tumors as a first clinical presentation related to BHD. BHD diagnosis also occurred at a later age in these patients (56 vs. 46 years) compared to those without presenting renal tumors. Median radiologic tumor size at first detection was 2 cm (range 0.5 to 12 cm), with clear cell renal carcinoma being the most common histopathological subtype. Independent risk factors for the development of renal tumors were older age and male sex, with shorter time to all-cause mortality for those with renal findings.

Table 3 Unadjusted and adjusted logistic regression model assessing risk of renal tumor development in patients with BHD

Variable	Univariable OR	95% CI	*P*-value	Multivariable OR	95% CI	*P*-value
Age at BHD diagnosis	1.04	1.01, 1.07	**0.003**	1.05	1.01, 1.08	**0.002**
	1	reference		1	reference	
Sex						
Male	2.58	1.21, 5.50	**0.01**	2.59	1.17, 5.73	**0.02**
Female	1	reference		1	reference	
Smoking						
Positive	2.60	1.19, 5.63	**0.02**	2.03	0.90, 4.60	0.09
Negative	1	Reference		1	reference	
FLCN gene mutation						
Positive	0.46	0.10, 2.04	0.31	0.43	0.84, 2.23	0.32
Negative	1	reference		1	reference	
Family history renal cancer						
Positive	0.65	0.26, 1.65	0.36	0.79	0.29, 2.15	0.64
Negative	1	reference		1	reference	
Presence of dermatological findings						
Positive	2.33	1.09, 4.99	**0.03**	2.30	1.01, 5.11	0.05
Negative	1	reference		1	reference	
Presence of lung cysts						
Positive	0.64	0.30, 1.37	0.15	0.68	0.30, 1.52	0.35
Negative	1	reference		1	Reference	
Presence of pneumothorax						
Positive	3.56	1.10,11.46	**0.03**	3.15	0.92,10.77	0.07
Negative	1	Reference			Reference	
Pulmonary function at time of BHD diagnosis						
FVC%	0.97	0.94, 1.01	0.12	0.97	0.94, 1.01	0.21
FEV1%	0.95	0.91, 1.0	**0.02**	0.95	0.91, 1.00	0.07
DLCO%	0.98	0.94, 1.01	0.19	1.0	0.96, 1.04	0.86

CI = confidence interval, BHD = Birt-Hogg- Dube´, FLCN = folliculin, %FVC = forced vital capacity,

%FEV1 = forced expiratory volume in first second, %DLCO = diffusion capacity for carbon monoxide

Prior studies have broadly reviewed renal tumor association and clinical presentation in BHD. Schmidt and colleagues assessed 219 individuals (110 females and 109 males) from 53 families and found 38 (17%, representing 24 BHD-affected families) diagnosed with renal tumors [10]. Males developed renal tumors more often than females (27 males vs. 11 females) with a median age of 48 years (range 31–71 years) at tumor diagnosis. Zbar and colleagues reported the odds of developing renal tumors as 7.3 times higher in patients with BHD than in unaffected individuals [11]. Age was associated with the development of renal tumors ($P=0.005$), noting 11.9% of patients older than 40 were diagnosed with renal tumors as compared to 2.3% of those younger than 40. Males were marginally twice as likely to develop tumors compared to females ($P=0.06$). Toro et al. reviewed 50 families with BHD and found 34% of individuals and 49% of families were diagnosed with renal tumors [12]. A seven-fold increase in the development of renal tumors was noted compared to unaffected individuals. Interestingly, men and women in their study had similar rates of renal tumor development with similarly varied radiologic presentations (bilateral, multifocal, or unilateral renal abnormalities). While we did not assess affected individuals as family cohorts, we found 26% of affected individuals in our cohort were diagnosed with renal tumors and at a slightly older age (53.6 years). Diagnosis of BHD appeared delayed in that setting, compared to those without renal abnormalities, despite similar presenting clinical characteristics.

We found age to be a significant predictor of renal tumor development, consistent with previous work highlighting age at onset anywhere between 45 and 55 in patients with BHD [13]. The youngest age at renal tumor diagnosis was 32 in our cohort, with the youngest reported in the literature at fourteen [14]. Our oldest patient was 82, consistent with Benusiglio et al. [15] who reported an incidental renal tumor in an 83-year-old. Current recommendations for surveillance suggest starting at the age of 20 [6] or 21 [5], though given the wide age range and often later tumor presentation, surveillance may need to continue through the fifth or sixth decade. Houweling et al. suggest a 16–20% risk of developing renal cancer in patients with BHD by the age of 70 [16]. Lastly, age at BHD diagnosis in our cohort was older (56 compared to 46.7) for those with renal tumor at

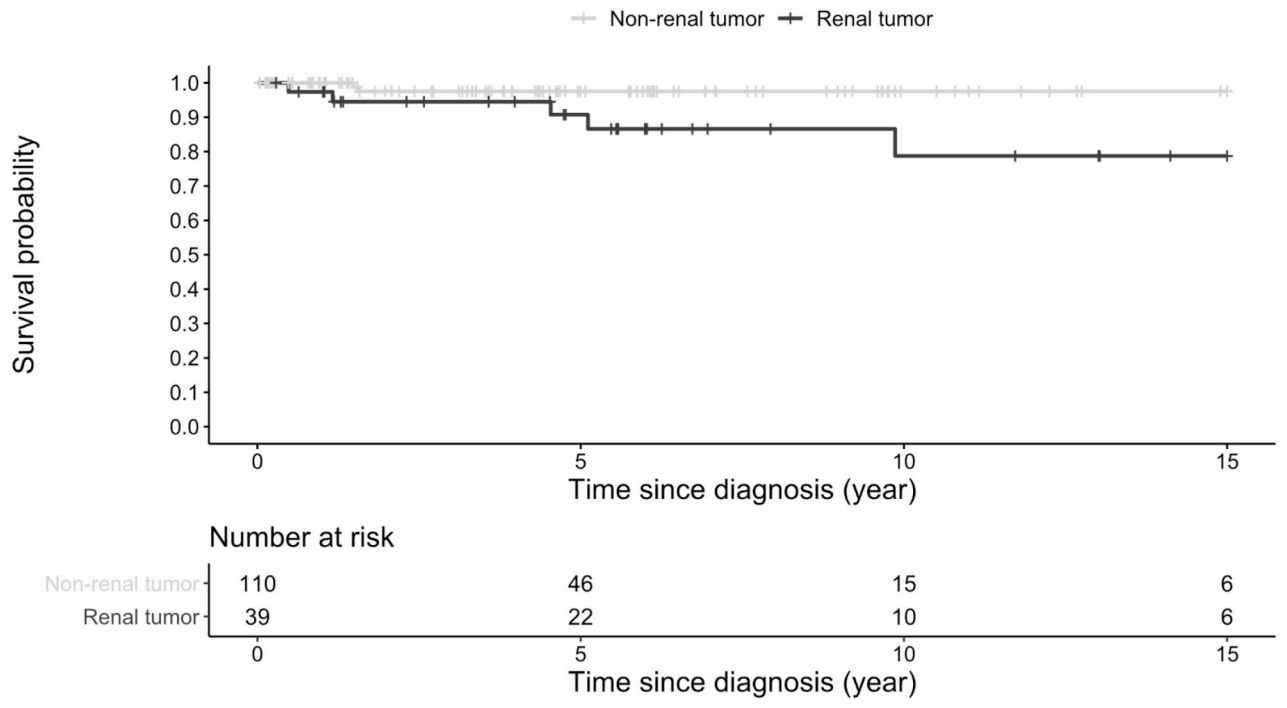

Fig. 2 Kaplan-Meier survival analysis stratified by presence of renal tumor (Log rank $P = 0.02$)

presentation. This suggests other clinical findings leading to suspicion of BHD (skin or pulmonary findings) are not well-recognized or occur later than in those with initial or subsequent tumor findings. Predominant initial clinical findings in the non-renal tumor group were lung cysts and skin manifestations, accounting for 47% and 21% of patients, respectively. Incidental renal abnormalities as a first sign of BHD occurred in 20 of 39 patients with renal tumors in our cohort. Toro et al. described 25% of patients presenting with fibrofolliculomas, pneumothoraces, and renal tumors at BHD diagnosis, while only 2% presented with renal tumors but no other clinical findings [12]. These variations may reflect the diverse skin, lung, and renal abnormalities seen both among individuals and within families affected by BHD, a well-recognized feature of the disorder.

Male sex is a known predictor of renal tumor development in non-BHD disease, with greater risk in men among the general population [17]. A prior systematic review of renal cell carcinoma found males were at higher risk of developing severe kidney cancer with worse outcomes. Although various genetic and molecular markers have been studied, the underlying biological mechanisms are still not fully understood [17]. The renal tumor group within our BHD cohort had a higher proportion of males (64%) with an OR of 2.68 for the development of renal tumors. This finding aligns with those of Pavlovich [18] and Benusiglio [15], who report a male predominance for renal tumors in patients with BHD. However, this contrasts with other BHD cohort studies reporting no sex predilection for renal tumors [13, 16].

An important aspect in the management of BHD is delineating an optimal interval for follow-up imaging in patients without initial renal abnormalities. As risk of tumor development is greater compared to unaffected individuals, timely detection and resection of smaller disease may be 'nephron-sparing' and minimize loss of renal function [19]. However, we observed only two cases in our cohort with renal tumors detected after BHD diagnosis, at two and seven years, respectively. Peak growth rate for renal tumors during the follow-up period was 0.23 centimeters per year. A prior study recommended imaging every three years in patients with normal radiologic findings at presentation, particularly younger patients [5]. The largest study to date assessing 199 genetically confirmed patients with BHD followed up to a median of 4.2 years diagnosed 23 new cases of subsequent renal tumors [13]. Abdominal CT was recommended as a relatively sensitive and cost-effective approach to screening, with 83% of patients completing at least yearly screening in the observation period. Unfortunately, regular monitoring with CT may expose patients to unnecessary radiation, making MRI a safer and lower-risk alternative.

Consistent with prior reports, most cases of BHD-related renal tumors were detected at earlier stages in our study [12]. We found only one patient with metastatic

disease after initial nephrectomy, undergoing resection, radiation, and immunotherapy. Houweling et al. [16] found 5 of 14 patients presenting with initial metastatic disease, while Benusiglio et al. [15] reported 4 of 33 patients with metastases, subsequently responsive to treatment. We found no cancer-associated deaths, however, others have described poorer prognosis in those with metastases [16, 20]. One explanation for our improved cancer-associated morbidity may be the immediate resection of tumors at the time of first detection (93%), including six with lesions less than 3 cm. Continued surveillance after resection may be relevant for detecting recurrence or occult metastases, though the timing or duration of this is difficult to ascertain from our findings or the current literature.

Our study has several limitations. First, data from a retrospective multi-site academic center may not account for differences in diagnostic approaches or management strategies compared to other academic or community practices, as highlighted by the earlier detection of renal abnormalities on imaging but delayed BHD diagnosis until tertiary referral, as seen in our study. A retrospective approach only accounts for association, but not causation of clinical findings, and with limited index cases, adjustment for covariables is limited. Lastly, despite the moderate sample size, a review of patients evaluated over two decades may not account for changes in disease screening or treatment that may impact long-term outcomes or related comorbidities.

In summary, we identified a cohort of patients with BHD highlighted by initial findings of renal tumors at presentation and diagnosis, with age and sex as independent predictors of tumor development. While cases of both older and younger patients have been reported in the literature, our findings are consistent with a median age at presentation among patients with BHD in their early to mid-50s. Current screening strategies, derived from other inherited or spontaneous renal tumor diseases, should account for this later presentation in BHD balancing a longer period of surveillance with earlier-stage detection and resection, the latter likely being a primary driver of improved outcomes in those with renal tumor development.

Abbreviations

BHD	Birt-Hogg-Dube´
BMI	Body mass index
CI	Confidence interval
CM	Centimeter
CT	Computed tomography
DLCO	Diffusing capacity for carbon monoxide
EMR	Electronic medical record
FEV1	Forced expiratory volume in the first second
FLCN	Folliculin gene
FVC	Forced vital capacity
IQR	Interquartile range
MRI	Magnetic resonance imaging
RCC	Renal cell carcinoma
SD	Standard deviation
UA	Urinalysis

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Author contributions
All authors contributed to study conceptualization, design, data abstraction, statistical analysis, and manuscript writing.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Mayo Clinic IRB approval was obtained before the initiation of any study activities.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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