World J Urol
DOI 10.1007/s00345-015-1583-7

ORIGINAL ARTICLE

Prognostic factors and outcomes in primary urethral cancer: results from the international collaboration on primary urethral carcinoma

Georgios Gakis[1] · Todd M. Morgan[2] · Jason A. Efstathiou[3] · Kirk A. Keegan[4] · Johannes Mischinger[1] · Tilman Todenhoefer[1] · Tina Schubert[1] · Harras B. Zaid[4] · Jan Hrbacek[5] · Bedeir Ali-El-Dein[6] · Rebecca H. Clayman[3] · Sigolene Galland[3] · Kola Olugbade Jr.[2] · Michael Rink[7] · Hans-Martin Fritsche[8] · Maximilian Burger[8] · Sam S. Chang[4] · Marko Babjuk[5] · George N. Thalmann[9] · Arnulf Stenzl[1] · Siamak Daneshmand[10]

Received: 15 March 2015 / Accepted: 28 April 2015

Abstract
Purpose To evaluate risk factors for survival in a large international cohort of patients with primary urethral cancer (PUC).
Methods A series of 154 patients (109 men, 45 women) were diagnosed with PUC in ten referral centers between 1993 and 2012. Kaplan–Meier analysis with log-rank test was used to investigate various potential prognostic factors for recurrence-free (RFS) and overall survival (OS). Multivariate models were constructed to evaluate independent risk factors for recurrence and death.
Results Median age at definitive treatment was 66 years (IQR 58–76). Histology was urothelial carcinoma in 72 (47 %), squamous cell carcinoma in 46 (30 %), adenocarcinoma in 17 (11 %), and mixed and other histology in 11 (7 %) and nine (6 %), respectively. A high degree of concordance between clinical and pathologic nodal staging (cN+/cN0 vs. pN+/pN0; $p < 0.001$) was noted. For clinical nodal staging, the corresponding sensitivity, specificity, and overall accuracy for predicting pathologic nodal stage were 92.8, 92.3, and 92.4 %, respectively. In multivariable Cox-regression analysis for patients staged cM0 at initial diagnosis, RFS was significantly associated with clinical nodal stage ($p < 0.001$), tumor location ($p < 0.001$), and age ($p = 0.001$), whereas clinical nodal stage was the only independent predictor for OS ($p = 0.026$).
Conclusions These data suggest that clinical nodal stage is a critical parameter for outcomes in PUC.

Keywords Clinical · Nodal stage · Primary urethral carcinoma · Prognostic · Risk factors · Survival

✉ Georgios Gakis
georgios.gakis@web.de; georgios.gakis@googlemail.com

[1] Department of Urology, University of Tübingen, Tübingen, Germany

[2] Department of Urology, University of Michigan, Ann Arbor, MI, USA

[3] Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

[4] Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN, USA

[5] Department of Urology, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic

[6] Mansoura Clinic, Urology and Nephrology Center, Mansoura, Egypt

[7] Department of Urology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

[8] Department of Urology, University Hospital Regensburg, Regensburg, Germany

[9] Department of Urology, University Hospital Berne, Berne, Switzerland

[10] USC/Norris Comprehensive Cancer Center, Institute of Urology, Los Angeles, CA, USA

Published online: 17 May 2015

Introduction

Primary urethral carcinoma (PUC) is a rare malignancy accounting for well under 1 % of all malignancies. The estimated annual incidence of PUC is 650 new cases in Europe with age-standardized ratio of 1.6/million in men and 0.6/million in women, and based on an analysis of the Surveillance, Epidemiology and End Results (SEER) registry, the age-standardized rate was reported to be approximately three times higher in the USA (4.3/million in men and 1.5/million in women) [1, 2].

Given the rarity of this cancer, there is a paucity of data regarding the relationship between prognostic factors and clinical outcomes. Therefore, optimizing treatment of advanced urethral cancer has recently become the focus of international healthcare authorities aiming to improve the oncological efficacy and quality of life of patients with PUC [3].

Since the majority of reports on prognostic factors in PUC are derived mainly from case series [3], there remain critical gaps in our understanding of how the underlying tumor biology affects clinical outcomes. In order to develop future treatment pathways and optimize the management of patients with PUC, there is an urgent clinical need to address the impact of clinical and histological risk factors on survival. For this reason, we have assembled a multi-institutional collaborative effort with the aim of determining the prognostic impact of clinical and pathologic risk factors in patients with PUC.

Patients and methods

In this Institutional Review Board-approved retrospective observational multicenter analysis, we reviewed the clinical and pathologic records of a total of 154 consecutive patients who were treated for PUC at ten tertiary academic centers between 1993 and 2012.

Clinical and histological assessment

The following clinical and pathologic parameters were assessed: age at primary treatment, gender, clinical and pathologic tumor stage, clinical and pathologic lymph node tumor involvement, underlying histology, tumor grade, tumor location (proximal vs. distal), prior history of malignancy, the presence of distant metastatic disease, modality of primary and salvage treatment, perioperative treatment, and preoperative serum creatinine level.

Clinical staging was based on preoperative bimanual examination and cross-sectional imaging findings. The histological assessment was performed at the center-specific pathology department and was based on the WHO-grading system and TNM classification as approved by the AJCC [4]. The pathologic macro- and microscopic evaluation of specimens included cross-sectioning of the entire specimen with immunohistochemical staining to identify the presence of urothelial, squamous cell, adenocarcinoma or other histological variants [5]. Clinical staging was based on biopsy, bimanual examination, and cross-sectional imaging findings. Patients with evidence of distant metastatic disease on cross-sectional imaging were excluded from survival analysis.

Treatment approach

The majority of patients underwent surgery for primary treatment, while only a small proportion was treated with radiotherapy and/or chemotherapy only (see Table 1). Surgery was conducted either by transurethral resection or by open excision using partial or total urethrectomy techniques in conjunction with radical cystectomy and urinary diversion, when necessary. Regional lymph node dissection (LND) was performed at the discretion of the treating surgeon based on intraoperative and preoperative cross-sectional imaging findings. The level of LND was based on the location of the primary tumor and typically included the inguinal lymph nodes, external and internal iliac, obturator, and common iliac lymph nodes.

Follow-up

Electronic hospital charts and physician records were reviewed to determine clinical outcomes. Patients generally were seen postoperatively at least every three to four months for the first year, semiannually for the second and third years, and annually thereafter. Follow-up examinations included cross-sectional imaging with computed tomography or magnetic resonance imaging. In addition to physical examination with laboratory testing, intravenous pyelography, cystoscopy, urine cytology, urethral washings, and bone scintigraphy were carried out, if indicated. Recurrence was defined as disease recurrence locally in the urethra, in lymph nodes or in distant organs.

Statistical analysis

For univariable analysis, Chi-square and Fisher's exact tests were used for nominal data and Student's *t* test for scaled data. Kaplan–Meier plots were used to estimate recurrence-free survival (RFS) and overall survival (OS) using log-rank testing. For determining RFS, clinical outcomes were measured from the date of primary treatment to the date of first documented recurrence. For RFS and OS, the date of recurrence/death was determined by cross-sectional imaging findings/death certificates or hospital charts, and

Table 1 Clinical and pathologic parameters in the 154 patients with primary urethral carcinoma

	Number of patients (%)
Gender	
Male	109 (70.8)
Female	45 (29.2)
Age	
Median	66
IQR	58–76
cT-stage	
cTa	20 (12.9)
cTis	8 (5.2)
cT1	48 (31.2)
cT2	42 (27.3)
cT3	23 (14.9)
cT4	13 (8.5)
pT-stage	
pT0	3 (2.2)
pTa	17 (12.9)
pTis	9 (6.9)
pTis (pu)	5 (3.8)
pTis (pd)	3 (2.3)
pT1	21 (15.9)
pT2	32 (24.2)
pT3	21 (15.9)
pT4	21 (15.9)
cN-stage	
cNX	26 (16.8)
cN0	104 (67.5)
cN+	24 (15.6)
pN-stage	
pNX	58 (43.9)
pN0	54 (40.9)
pN1	4 (3.0)
pN2	16 (12.1)
Tumor grade	
G1	10 (6.5)
G2	33 (21.4)
G3	93 (60.4)
GX	8 (5.2)
Not available	10 (6.5)
Histology	
UC	72 (46.8)
SCC	46 (29.9)
AC	17 (11.0)
Mixed (UC ± SCC ± AC)	11 (7.1)
Melanoma	4 (2.6)
Leiomyosarcoma	2 (1.3)
Adenoid cystic carcinoma	1 (0.7)
Sarcomatoid	1 (0.7)
Tumor location	
Men	
Prostatic	41 (37.6)
Membranous	7 (4.6)
Bulbar	11 (10.1)
Penile	29 (26.6)
Distal	10 (9.2)
Women	
Proximal	13 (28.9)
Distal	31 (68.9)
Proximal plus distal	
Men	11 (10.1)
Women	1 (2.2)
Tumor size (cm)	
Mean	2.8
Median	2
IQR	1–4.6
Distant metastasis at primary diagnosis	
cM0	125 (81.8)
cM1	29 (18.8)
Prior history of malignancy	
Present	34 (22.1)
Absent	120 (77.9)
Per cancer entity	
Prostate	14 (9.1)
Breast	5 (3.3)
Lung	4 (2.6)
Colorectal	2 (1.3)
Kidney	3 (2.0)
Testicular	1 (0.7)
Vulvar	1 (0.7)
Vaginal	1 (0.7)
Uterus	1 (0.7)
Oropharyngeal	1 (0.7)
Lymphoma	1 (0.7)
Pretreatment serum creatinine level (mg/dl)	
Median	1.0
Mean	1.0
IQR	0.8–1.2
Perioperative treatment	
Neoadjuvant chemotherapy	16 (10.4)
Neoadjuvant chemoradiotherapy	9 (5.8)
Adjuvant chemotherapy	23 (14.9)
Modality of primary treatment	
TUR urethra	38 (24.7)
Transurethral laser resection	1 (0.6)
Partial urethrectomy	6 (3.9)
Urethrectomy	39 (25.3)
Prostatectomy	1 (0.6)
Cyst(oprostat)ectomy plus urethrectomy	43 (27.9)

Table 1 continued

	Number of patients (%)
Supravesical diversion only	1 (0.6)
Radiotherapy	3 (1.9)
Chemotherapy	4 (2.6)
Chemoradiotherapy	9 (5.8)
Other	9 (5.8)
Modality of salvage treatment for recurrence	
Surgery	32 (20.8)
Radiotherapy	8 (5.2)
Surgery and radiotherapy	5 (3.3)
Location of recurrence	
LN	18 (11.7)
Distant	5 (3.3)
Urethral	28 (18.2)
LN plus distant	12 (7.8)
LN plus urethral	6 (3.9)
Distant plus urethral	4 (2.6)
LN plus distant plus urethral	9 (5.8)
No recurrence	72 (46.8)

ACH adjuvant chemotherapy, *BSC* best supportive care, *IQR* interquartile range, *NAC* neoadjuvant chemotherapy, *N-CRT* neoadjuvant chemoradiotherapy, *TUR* transurethral resection, *pu* prostatic urethra, *pd* prostatic ducts, *LN* lymph nodes

patients still alive/without evidence of recurrence were censored on the date of last follow-up [6].

Multivariable Cox-regression analysis was used to investigate independent risk factors for RFS and OS. p values are two-sided, and $p < 0.05$ was considered significant. Statistical analysis was performed using JMP® 11.0. Values are given as mean, median, and interquartile range (IQR).

Results

Clinical and pathologic tumor and patient characteristics are listed in Table 1. Of the 154 patients, 109 (70.8 %) were men and 45 (29.2) women. The median age at definitive treatment was 66 years (IQR 58–76). The predominant underlying histological entities were urothelial carcinoma in 72 (46.8 %), squamous cell carcinoma in 46 (29.9 %), and adenocarcinoma in 17 (11.0 %) patients, respectively. In men, tumors were located in the proximal, distal, and proximal plus distal urethra in 54.1, 35.8, and 10.1 %, respectively. Conversely, in women, tumors were located in the proximal, distal, and proximal plus distal urethra in 28.9, 68.9, and 2.2 %, respectively ($p = 0.22$). Distant metastatic disease was present at initial diagnosis in 29 patients (18.8 %).

Clinical nodal stage was cN0 in 104 (75.5 %), cN1 in 24 (15.6 %), and cNX in 28 patients (18.2 %). In the patients who underwent LND, the median number of removed lymph nodes was 15 (IQR 4–21). Pathologic nodal stage was pN0 in 54 and pN1-2 in 20. In these 74 patients, a high degree of concordance between clinical and pathological nodal staging (cN+/cN0 vs. pN+/pN0; $p < 0.001$) was noted. For clinical nodal staging, the corresponding sensitivity, specificity, and overall accuracy for predicting pathologic nodal stage were 92.8, 92.3, and 92.4 %, respectively.

In the total cohort, the mean follow-up was 32 months (median 21 months; IQR 5–48). The location of recurrence/metastatic disease in the 154 patients is listed in Table 1. Recurrence was documented in 82 of the 154 patients (53.3 %). The corresponding three-year RFS was 60.8 %. Of the 125 patients with cM0 disease, 40 (26.0 %) died with a corresponding to three-year OS of 80.4 %.

The exact modalities of perioperative chemo-/radiotherapy, primary and salvage treatments are listed in Table 1. In univariable analysis, overall recurrence was significantly associated with pathologically advanced tumor stage (≥pT3, $p = 0.001$), clinically and pathologically node-positive disease ($p = 0.001$ and $p = 0.006$), as well as proximal tumor location ($p = 0.002$). No significant associations were found between recurrence and tumor size ($p = 0.06$), age, gender, clinical tumor stage, tumor grade, prior history of malignant disease, pretreatment serum creatinine level, and histological subtype (see Table 2).

In univariable analysis for patients staged cM0 at initial diagnosis, overall death was significantly associated with pathologically advanced tumor stage ($p = 0.044$), clinically and pathologically node-positive disease ($p = 0.036/0.014$), and tumor grade ($p = 0.029$; see Table 2).

In multivariable Cox-regression analysis, RFS was significantly associated with clinical nodal stage ($p < 0.001$), tumor location ($p < 0.001$), and age ($p = 0.001$), whereas clinical nodal stage was the only independent predictor for OS ($p = 0.026$). No significant associations were found in uni- and multivariable analyses between overall death and clinical tumor stage, age, gender, tumor location and size, prior history of malignant disease, pretreatment serum creatinine level, and histology (see Table 3).

Discussion

Since PUC is a rare tumor entity, the prognostic significance of clinical and pathologic risk factors prior initiation of primary treatment is uncertain. For this reason, we established a collaborative database and accrued a total of 154 cases to inform about primary characteristics and the prognostic role of clinical and pathologic risk factors for survival in PUC.

In the present analysis, the male-to-female ratio was 2.4:1, and urothelial carcinoma was found to be the

Table 2 Univariable analysis for recurrence-free and overall survivals in the 125 cM0 patients according to clinical and pathologic tumor characteristics

Parameter	RFS		OS	
	RR (95 %-CI)	*p* value	RR (95 %-CI)	*p* value
Pathologic tumor stage	2.77	**0.001**	2.80	**0.044**
≥pT3 versus ≤pT2	(1.54–4.88)		(1.03–7.19)	
Pathologic nodal stage	3.74	**0.006**	3.50	**0.014**
pN+ versus pN0/pNX	(1.51–8.04)		(1.06–15.74)	
Clinical tumor stage	1.62	0.14	1.78	0.24
≥cT3 versus ≤cT2	(0.83–2.98)		(0.64–4.36)	
Clinical nodal stage	4.01	**0.001**	3.98	**0.036**
cN+ versus cN0	(1.93–7.78)		(1.10–11.59)	
Tumor location	2.33	**0.002**	2.22	0.06
Proximal versus distal	(1.33–4.29)		(0.94–5.82)	
Tumor grade	1.50	0.18	3.01	**0.029**
G3 versus G1/G2	(0.82–2.87)		(1.11–10.52)	
Histology	1.06	0.89	1.06	0.89
UC versus non-UC	(0.45–2.62)		(0.45–2.62)	
Gender	1.20	0.53	0.91	0.82
Male versus female	(0.68–2.25)		(0.39–2.28)	
Age				
(Continuously coded; total risk range)	2.43 (0.54–11.33)	0.23	2.10 (0.28–19.59)	0.48
≥65 years versus <65 years	1.13 (0.61–2.14)	0.69	1.15 (0.47–2.87)	0.75
Serum creatinine level				
(Continuously coded; total risk range)	0.93 (0.11–6.84)	0.94	0.77 (0.04–11.93)	0.86
Elevated versus normal	0.98 (0.44–2.61)	0.96	0.90 (0.32–3.21)	0.85
Tumor size (cm)				
(Continuously coded; total risk range)	5.99 (0.90–38.64)	0.06	1.84 (0.11–26.80)	0.66
Prior history of malignoma	1.33	0.43	1.96	0.18
Present versus absent	(0.63–2.64)		(0.71–5.11)	

Bold values indicate statistically significant difference. Elevated serum creatinine was defined in men as >1.1 mg/dl and in women >0.8 mg/dl

CI confidence interval, *OS* overall survival, *RFS* recurrence-free survival, *RR* relative risk, *UC* urothelial carcinoma

predominant histological entity in approximately 47 % of the patients. These findings are in line with prior studies [2, 7, 8]. Clinically advanced tumor stage was present in approximately one-fourth of the patients. Since our study covers a period of 20 years, we were not able to retrospectively adjust for the distinct method used for tumor imaging [computed tomography vs. magnetic resonance imaging (MRI)] at primary diagnosis. However, for improved evaluation of local tumor extent, MRI has been shown to provide superior soft tissue contrast compared with computed tomography [9], which is also recommended by recent guidelines [3]. In this regard, we found a very high accuracy of ~93 % for clinical nodal staging to predict pathological lymph node involvement. This finding is in line with prior studies reporting enlarged lymph nodes in PUC to be often associated with lymph node metastatic disease [3, 10]. The high accuracy for clinical nodal staging may also be in part due to the fact that the inguinal regions represent the primary lymphatic landing sites of distal urethral tumors which are easily assessable by clinical palpation and cross-sectional imaging. With regard to the high degree of concordance between clinical and pathologic staging, these data suggest that the presence of clinically enlarged lymph nodes should alert clinicians of the possible presence of lymph node metastases and should therefore be an impetus to consider a multimodal approach [3, 10].

In this study, most tumors were of higher grade and were located in the proximal urethra in approximately two-thirds

Table 3 Multivariable analysis of clinical and pathologic parameters available prior definitive treatment for predicting recurrence and overall death in the 125 patients with cM0 primary urethral carcinoma

RFS			OS	
Variable	Hazard ratio (95 %-CI)	*p* value	Hazard ratio (95 %-CI)	*p* value
Clinical tumor stage	2.04	0.40	1.17	0.85
≥cT3 versus ≤cT2	(0.41–13.09)		(0.19–5.69)	
Clinical nodal stage	**48.64**	**<0.001**	**9.80**	**0.026**
cN+ versus cN0/cNX	**(6.96–509.50)**		**(1.31–92.37)**	
Tumor location	**10.32**	**<0.001**	1.70	0.47
Proximal versus distal	**(2.47–72.91)**		(0.41–8.80)	
Tumor grade	1.11	0.86	4.11	0.08
G3 versus G1/G2	(0.31–4.03)		(0.84–24.97)	
Histology	0.70	0.46	1.41	0.56
UC versus non-UC	(0.27–1.80)		(0.44–4.89)	
Gender	2.70	0.08	1.71	0.39
Male versus female	(0.89–9.16)		(0.50–6.36)	
Age	**7.17**	**0.001**	1.96	0.31
≥65 years versus <65 years	**(2.18–26.33)**		(0.52–7.48)	
Prior history of malignoma	1.05	0.94	2.14	0.27
Present versus absent	(0.25–4.07)		(0.55–9.03)	

Bold values indicate statistically significant difference

of the men and in one-third of the women. The median tumor size was 2 cm. Of note, 29 of the 154 patients presented with metastatic disease at distant organs, and 34 patients (22 %) had a prior history of malignant disease. The most predominant type of prior malignancy was prostate cancer. However, as this series is retrospective, we cannot accurately adjust for any causative association between the primary treatment for these malignancies and the carcinogenesis of PUC.

As would be expected, recurrence was significantly associated with advanced clinical nodal stage, advanced pathological tumor, and nodal stage and proximal tumor location. Similarly, OS was significantly associated with clinical nodal stage, pathologic tumor, and nodal stage and tumor grade. These results are in accordance with prior studies [2, 7, 8]. For multivariable analysis, we decided to include only clinical and pathologic parameters that are available before initiation of primary treatment in order to make the analysis more useful for clinical decision-making. For this reason, we included clinical tumor and nodal stage instead of the respective (postoperative) pathologic determinants for primary tumor extent. Clinical nodal stage, tumor location, and age were found to be independently predictors for RFS, whereas clinical nodal stage was the only independent predictor for OS. In line with prior studies [1, 2, 7, 8], we did not find gender or histological subtype to impact survival. Our results are supported by an analysis of the SEER registry conducted exclusively in women with PUC demonstrating that node-positive disease was also an independent predictor for inferior survival [11]. Preoperative renal function did not impact on RFS and OS. These data strongly suggest that nodal stage is the most critical parameter in primary urethral carcinoma. In terms of the oncologic effects of neoadjuvant chemotherapy and salvage treatment, we have investigated their impact on survival in recent analyses. Patients with clinically advanced tumor stages (cT3 and/or cN+) benefited most from neoadjuvant chemotherapy [12]. Likewise patients undergoing salvage surgery or radiotherapy for local recurrence exhibited improved overall survival compared with those who did not undergo salvage treatment for recurrence [13].

Our study has several limitations inherent to its retrospective and multicenter nature which is, of course, requisite to the rarity of this cancer entity. Although we included patients treated at academic centers in Europe and North America within the last 20 years, the number of included patients is moderate, and follow-up period is short which is due to the rarity and aggressiveness of the disease. Further biases include the absence of regional LND in approximately half of the patients and possible interobserver variability in the clinical staging and pathological assessment of specimens. We could not adjust for possible heterogenous practice patterns in the different institutions, patient preferences, toxicities and side effects of treatment, as well as comorbidities which may have impacted on the clinical decision-making. In this regard, survival may also have been impacted by the ability of patients to undergo chemotherapy prior to surgery. Yet, preoperative serum creatinine levels did not exert an impact on RFS and OS. In addition, all patients were treated in academic centers by

multidisciplinary teams dedicated to the management of urinary tract cancers. In line with the updated 2015 EAU Guidelines on Primary Urethral Carcinoma [10], we would like to reinforce that patients with urethral carcinomas should be treated in academic centers. As urethral carcinomas are rare and aggressive cancers, patients should be referred to institutions with multidisciplinary teams. Notwithstanding these limitations, this study represents one of the largest studied cohorts of primary urethral carcinomas that systematically has investigated the impact of clinical and pathologic tumor characteristics on outcomes.

Conclusions

In this series, clinical nodal stage, tumor location, and age were found to be independent predictors of RFS in primary urethral carcinoma, whereas clinical nodal stage was the only independent predictor of OS.

Conflict of interest None.

Ethical standard This is an IRB-approved study conducted according to the Declaration of Helsinki.

References

1. Visser O, Adolfsson J, Rossi S et al (2011) The RARECARE working group. incidence and survival of rare urogenital cancers in Europe. Eur J Cancer 48:456–464. doi:10.1016/j.ejca.2011.10.031
2. Swartz MA, Porter M, Lin DW, Weiss NS (2006) Incidence of primary urethral carcinoma in the United States. Urology 68:1164–1168
3. Gakis G, Witjes JA, Compérat E et al (2013) EAU guidelines on primary urethral carcinoma. Eur Urol. doi:10.1016/j.eururo.2013.03.044
4. Sobin LH, Wittekind C (2002) TNM classification of malignant tumors, 6th edn. Wiley-Liss, New York
5. Shim JW, Cho K, Choi YD et al (2008) Diagnostic algorithm for papillary urothelial tumors in the urinary bladder. Virchows Arch 452:353–362
6. Rink M, Fajkovic H, Cha EK et al (2012) Death certificates are valid for the determination of cause of death in patients with upper and lower tract urothelial carcinoma. Eur Urol 61:854–855
7. Derksen JW, Visser O, de la Rivière GB, Meuleman EJ, Heldeweg EA, Lagerveld BW (2012) Primary urethral carcinoma in females: an epidemiologic study on demographical factors, histological types, tumour stage and survival. World J Urol 31:147–153
8. Rabbani F (2011) Prognostic factors in male urethral cancer. Cancer 117:2426–2434
9. Gourtsoyianni S, Hudolin T, Sala E, Goldman D, Bochner BH, Hricak H (2011) MRI at the completion of chemoradiotherapy can accurately evaluate the extent of disease in women with advanced urethral carcinoma undergoing anterior pelvic exenteration. Clin Radiol 66:1072–1078
10. Gakis G, Witjes JA, Comperat E et al (2015) Guidelines on primary urethral carcinoma. In: European association of urology (ed) EAU Guidelines Office, Arnhem, pp 1–14
11. Champ CE, Hegarty SE, Shen X et al (2012) Prognostic factors and outcomes after definitive treatment of female urethral cancer: a population-based analysis. Urology 80:374–381
12. Gakis G, Morgan TM, Daneshmand S et al (2015) Impact of perioperative chemotherapy on survival in patients with advanced primary urethral cancer. Results of the international collaboration on primary urethral carcinoma. Ann Oncol. doi:10.1093/annonc/mdv230
13. Gakis G, Morgan TM, Daneshmand S et al (2015) Impact of salvage surgery and radiotherapy on survival in patients with recurrent primary urethral cancer. J Clin Oncol 33:5s (suppl; abstr 4568)