

Cancer Association of South Africa (CANSA)

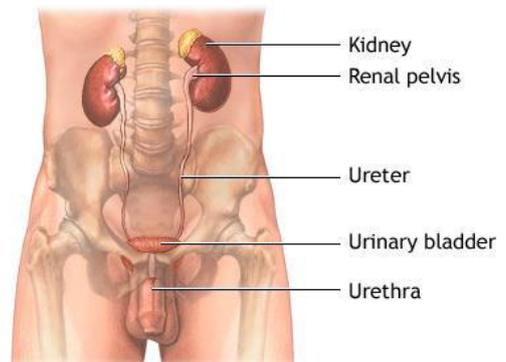


Fact Sheet on Bladder Cancer

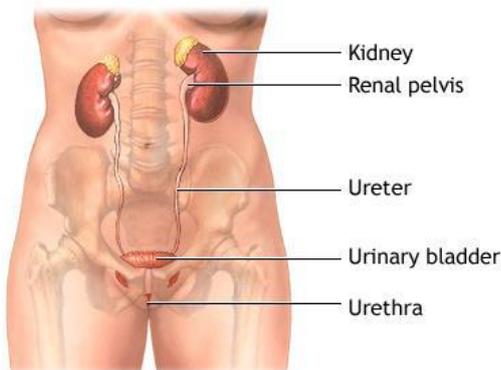
Introduction

The urinary bladder is the organ that collects urine excreted by the kidneys before disposal by means of urination. It is a hollow muscular, and distensible (elastic) organ. The bladder is situated on the pelvic floor. Urine enters the bladder via the ureters and exits via the urethra.

[Picture Credit: Male Urinary Tract]



ADAM.



[Picture Credit: Female Urinary Tract]

ADAM.

Bladder Cancer

Bladder cancer is cancer that forms in tissues of the bladder. Most bladder cancers are transitional cell carcinomas (cancer that begins in cells that normally make up the inner lining of the bladder). Other types include squamous cell carcinoma (cancer that begins in thin, flat cells) and adenocarcinoma (cancer that begins in cells that make and release mucus and other fluids).

Smith, A.B., Jaeger, B., Pinheiro, L.C., Edwards, L.J., Tan, H.J., Nielsen, M.E. & Reeve, B.B. 2018.

OBJECTIVES: To identify changes in health-related quality of life (HRQoL) after diagnosis of bladder cancer in older adults in comparison with a group of adults without bladder cancer (controls).

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

PATIENTS AND METHODS: Data from the Surveillance, Epidemiology and End Results registries were linked with Medicare Health Outcomes Survey (MHOS) data. Medicare beneficiaries aged ≥65 years in the period 1998-2013, who were diagnosed with bladder cancer between baseline and follow-up through the MHOS, were matched with control subjects without cancer using propensity scores. Linear mixed models were used to estimate predictors of HRQoL changes.

RESULTS: After matching, 535 patients with bladder cancer (458 non-muscle-invasive bladder cancer [NMIBC] and 77 with muscle-invasive bladder cancer [MIBC]) and 2 770 control subjects without cancer were identified. Both patients with NMIBC and those with MIBC reported significant declines in HRQoL scores over time vs controls: physical component summary -2 and -5.3 vs -0.4, respectively; bodily pain -1.9 and -3.6 vs -0.7; role physical -2.7 and -4.7 vs -0.7; general health -2.4 and -6.1 vs 0; vitality -1.2 and -3.5 vs -0.1; and social functioning -2.1 and -5.7 vs -0.8. All scores ranged from 0 to 100. When stratified by time since diagnosis, HRQoL improved over 1 year for some domains (role physical), but remained lower across most domains.

CONCLUSIONS: After diagnosis, patients with bladder cancer experienced significant declines in physical, mental and social HRQoL relative to controls. Decrements were most pronounced among individuals with MIBC. Methods to better understand and address HRQoL decrements among patients with bladder cancer are needed.

Incidence of Bladder Cancer in South Africa

According to the National Cancer Registry (2014) the following number of bladder cancer cases was histologically diagnosed in South Africa during 2014:

Group - Males 2014	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	942	1:152	2,56%
Asian males	44	1:93	4,70%
Black males	164	1:597	1,48%
Coloured males	143	1:76	3,41%
White males	591	1:60	2,87%

Group - Females 2014	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	337	1:654	0,89%
Asian females	14	1:480	1,19%
Black females	121	1:1 283	0,75%
Coloured females	42	1:470	1,03%
White females	160	1:256	0,97%

The frequency of histologically diagnosed cases of bladder cancer in South Africa for 2014 was as follows (National Cancer Registry, 2014):

Group - Males 2014	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	4	2	15	59	152	282	288	131
Asian males	0	0	1	1	7	18	15	1
Black males	3	0	5	21	37	50	24	14
Coloured males	1	1	4	9	30	42	36	18
White males	0	1	5	26	75	169	208	964

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

Group - Females 2014	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	2	1	18	43	56	84	77	51
Asian females	0	0	0	1	7	2	3	1
Black females	1	1	13	21	26	32	10	11
Coloured females	0	0	1	3	7	11	15	5
White females	1	0	3	18	16	39	49	33

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Risk Factors for Bladder Cancer

The following are risk factors for bladder cancer:

- Use of tobacco products
- Obesity
- Increasing age
- Being white
- Being a male
- Exposure to certain chemicals
- Previous cancer treatment
- Chronic bladder inflammation
- Schistosomiasis (Bilharzia)
- Personal or family history of cancer
- Bladder birth defects
- Inherited gene mutations
- Low fluid consumption

Signs and Symptoms of Bladder Cancer

People with bladder cancer may experience the following symptoms or signs:

- blood in urine (haematuria) — urine may appear dark yellow, bright red or cola coloured.
- frequent urination
- urgent need to urinate
- bladder spasm
- painful urination (dysuria)
- inability to urinate
- reduced bladder capacity
- back pain
- pelvic pain

Symptoms of advanced bladder cancer may include:

- pain
- unexplained appetite loss
- weight loss

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

Diagnosis of Bladder Cancer

Bladder cancers are usually found when a person goes to the doctor because of signs or symptoms they are having. If bladder cancer is suspected, tests will be needed to confirm the diagnosis.

- blood in the urine
- changes in bladder habits or irritating symptoms such as:
 - having to urinate more often than usual
 - feeling pain or burning during urination
 - feeling as if one needs to go right away, even when the bladder is not full
- medical history and physical exam
- urine culture
- urine tumour marker test
- biopsy
- intravenous pyelogram
- retrograde
- computed tomography (CT) scan
- magnetic resonance imaging (MRI) scan - Like CT scans but MRI scans use radio waves and strong magnets instead of x-rays
- ultrasound - uses sound waves to create pictures of internal organs

Bodgi, L., Bahmad, H.F., Arail, T., Al Chobog, J., Bou-Gharios, J., Cheaito, K., Zeidan, Y.H., Eid, T., Geara, F. & Abou-Kheir, W. 2019.

Background: Bladder cancer is the fourth most commonly diagnosed cancer among males worldwide. Current treatment strategies established for bladder cancer mainly consist of cystectomy yet advances in radiation therapy have pointed to the value of organ-preserving strategies in preserving patients' quality of life.

Aim: To study and compare the radiosensitivity in two-dimension (2D) and physiologically-relevant three-dimension (3D) *in vitro* culture of three human bladder cancer cell lines, RT4, T24, and UM-UC-3.

Materials and Methods: Clonogenic assay was performed to assess cells' radiosensitivity in 2D. Employing the 3D Matrigel™-based cultures to enrich for cancer stem cells (CSCs) allowed us to assess the survival of this subpopulation of cells via evaluating the number, i.e., sphere forming unit (SFU), and the sizes of cultured spheres, formed from cells exposed to different radiation doses compared to non-irradiated cells.

Results: Irradiating cells with increasing radiation doses revealed highest survival rates with RT4 cells in 2D, followed by T24 and UM-UC-3. In 3D, however, UM-UC-3 cells were shown to be the most radio-resistant as evidenced by the number of spheres formed, yet they displayed the least efficient volume reduction/regression (VR), whilst the volume decreased significantly for both RT4 and T24 cells. Sphere VR and sphere ratio (SR) values were then plotted against each other demonstrating a linear correlation between volume and number with RT4 and UM-UC-3 cell lines, but not T24. Lastly, multiple regression model was employed to evaluate the possibility of obtaining a function combining both 3D parameters, SR and VR, with the surviving fraction (SF) in 2D, and showed a linear regression for T24 cells only, with a correlation coefficient of 0.97 for the combined parameters.

Conclusion: We were able to radiobiologically characterize 3 human bladder cancer cell lines showing differential effects of radiation between 2D and 3D culture systems, paving the way for achieving better assessment of radiosensitivity of bladder cancer *in vitro*.

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

Kim, H.S., Kwak, C., Kim, H.H. & Ku, J.H. 2019.

OBJECTIVES: To validate the Cancer of the Bladder Risk Assessment (COBRA) score for predicting cancer-specific survival (CSS) in comparison with the American Joint Committee on Cancer (AJCC) staging system using an external cohort of urothelial carcinoma of the bladder (UCB) from South Korea.

MATERIALS AND METHODS: The final validation cohort consisted of 855 patients who underwent radical cystectomy (RC) for UCB in a single institution. The impact of the COBRA score on CSS was estimated using Cox proportional hazard models. Discrimination accuracy was quantified with concordance index. Calibration plots were used to determine the relationship between model-predicted CSS and actual CSS at 2years and 5years after RC. Clinical usefulness of the COBRA score was assessed using decision curve analyses.

RESULTS: One-point increase in the COBRA score (range, 0-6) was closely related to a 1.50-fold increase (95% confidence interval [CI]: 1.39-1.62) in the risk of death from UCB. Discrimination accuracies of the COBRA score and AJCC staging system for CSS at 5years were 70.6% (95% CI: 67.2-74.0) and 68.3% (95% CI: 65.0-71.6), respectively. Compared to the AJCC staging system, the COBRA score was generally well-calibrated for predicting CSS at 2 and 5years after RC. On decision curve analyses, the use of the COBRA score showed more clinical net benefits across a wide range of threshold probabilities than the AJCC staging system.

CONCLUSIONS: Our external validation results suggest that although the COBRA score is not perfectly accurate, it shows a reasonable level of discriminative ability, adequate calibration, and meaningful net benefit gain for predicting CSS after RC in a Korean UCB cohort.

Types of Bladder Cancer

Types of bladder cancer include:

Transitional cell bladder cancer

- Non muscle invasive (superficial) bladder cancer
- Invasive bladder
- Squamous cell bladder cancer
- Adenocarcinoma of the bladder
- Small cell cancer of the bladder - it is very rare

Reducing the Risk for Bladder Cancer

Bladder cancer cannot be prevented altogether, but one can reduce the risk for getting it:

- Do not smoke
- avoid exposure to industrial chemicals
- drink water throughout the day
- limit the intake of smoked or cured meats
- limit the intake of other processed foods

Staging of Bladder Cancer

The TNM staging system is used.

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

TNM is an abbreviation for tumour (**T**), node (**N**), and metastasis (**M**). Doctors look at these three factors to determine the stage of cancer:

- How large is the primary tumour and how deeply has it invaded the tissue? (**Tumour, T**)
- Has the tumour spread to the lymph nodes? (**Node, N**)
- Has the cancer spread (metastasised) to other parts of the body? (**Metastasis, M**)

Where Bladder Cancer Spreads to

Should bladder cancer spread to other parts of the body, it would most probably spread as indicated below:

Cancer Type:	Main Sites of Metastasis (Spread)
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colon	Liver, lung
Colorectal	Liver, lung, peritoneum (lining of abdomen)
Kidney	Adrenal gland, bone, brain, liver, lung
Lung	Adrenal gland, bone, brain, liver, other lung
Melanoma	Bone, brain, liver, lung, skin, muscle
Ovary	Liver, lung, peritoneum (lining of abdomen)
Pancreas	Liver lung, peritoneum (lining of abdomen)
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum (lining of abdomen), ovaries
Thyroid	Bone, liver, lung
Uterus	Bone, liver, lung, peritoneum (lining of abdomen), vagina
Non-melanoma skin cancer	Very rare: lymph nodes, lung, bone (if in head/neck region)

Treatment of Bladder Cancer

The following comprises standard treatment for bladder cancer:

- Surgery - one of the following types of surgery may be done:
 - Transurethral resection (TUR) with fulguration
 - Radical cystectomy (surgical removal of the bladder)
 - Segmental cystectomy (surgical removal of part of the bladder)
 - Urinary diversion - surgery to make a new way for the body to store and pass urine
- Radiation therapy
- Chemotherapy
- Biologic therapy
- Photodynamic therapy
- Immunotherapy

Mao, W., Ma, B., Huang, X., Gu, S., Luo, M., Fan, J. & Geng, J. 2019.

PURPOSE: We sought to identify the method that could obtain the best survival rate for AJCC stage IV bladder cancer (BCa) patients.

METHODS: Patients with AJCC stage IV BCa diagnosed between 2004 and 2015 were identified using the Surveillance, epidemiology and end results (SEER) database. Kaplan-Meier curves and log-rank test were used for overall survival (OS) and cancer-specific survival (CSS). Multivariable Cox

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

regression was used to determine factors associated with all-cause mortality (ACM) and cancer-specific mortality (CSM).

RESULTS: We found that among the 11824 patients, the number of patients who received chemotherapy (CT), radiotherapy (RT) and radical cystectomy (RC) was 6243 (52.8%), 2005 (17.0%) and 4987 (42.2%), respectively. Patients who received CT or RC had improved OS (26.4% vs. 11.7%, $p < 0.001$ and 27.3% vs. 13.7%, $p < 0.001$, respectively), but patients who underwent RT alone had lower OS (14.4% vs. 20.5%, $p < 0.001$). Furthermore, CT combined with RC was associated with the lowest ACM (hazard ratio (HR) = 0.26, 95% CI 0.24-0.28, $p < 0.001$) and the lowest CSM (HR = 0.24, 95% CI 0.22-0.26, $p < 0.001$). Patients who only received RT had the highest ACM (HR = 0.84, 95% CI 0.77-0.92, $p < 0.001$) and the highest CSM (HR = 0.85, 95% CI 0.77-0.94, $p = 0.002$).

CONCLUSIONS: We concluded that CT combined with RC was the best method with the highest survival rate for patients with AJCC stage IV BCa and that CT combined with RC had more benefits in improving OS and CSS than did RT alone.

Flannery, K., Boyd, M., Black-Shinn, J., Robert, N., Kamat, A.M. 2019.

AIM: Investigate the effectiveness of chemotherapy for first-line (1L) treatment of metastatic bladder cancer (mBC).

METHODS: Retrospective cohort study evaluating treatment patterns/outcomes in 1155 mBC patients receiving initial treatment in the community practice setting from January 2010 to June 2014, and followed through July 2016.

RESULTS: The most commonly utilized 1L and second-line (2L) regimens were platinum-based and taxane-based, respectively. Median (95% CI) OS for all patients from 1L initiation was 12.8 months (11.7-14.6), and median OS for all 2L regimens was 9.4 months (8.2-11.1).

CONCLUSION: mBC patients eligible for and who received cis-based regimens experienced better OS results. Poor renal function was a key driver of cis-ineligibility. The various monotherapy and combination chemotherapy regimens in 2L produced relatively short OS outcomes.

Häggström, C., Garmo, H., de Luna, X., Van Hemelrijck, M., Söderkvist, K., Aljabery, F., Ströck, V., Hosseini, A., Gårdmark, T., Malmström, P.U., Jahnson, S., Liedberg, F. & Holmberg, L. 2019.

BACKGROUND: Studies of survival comparing radical cystectomy (RC) and radiotherapy for muscle-invasive bladder cancer have provided inconsistent results and have methodological limitations. The aim of the study was to investigate risk of death after radiotherapy as compared to RC.

METHODS: We selected patients with muscle-invasive urothelial carcinoma without distant metastases, treated with radiotherapy or RC from 1997 to 2014 in the Bladder Cancer Data Base Sweden (BladderBaSe) and estimated absolute and relative risk of bladder cancer death and all-cause death. In a group of patients, theoretically eligible for a trial comparing radiotherapy and RC, we calculated risk difference in an instrumental variable analysis. We have not investigated chemoradiotherapy as this treatment was not used in the study time period.

RESULTS: The study included 3 309 patients, of those 17% were treated with radiotherapy and 83% with RC. Patients treated with radiotherapy were older, had more advanced comorbidity, and had a higher risk of death as compared to patients treated with RC (relative risks of 1.5-1.6). In the "trial population," all-cause death risk difference was 6 per 100 patients lower after radiotherapy at 5 years of follow-up, 95% confidence interval -41 to 29.

CONCLUSION(S): Patient selection between the treatments make it difficult to evaluate results from conventionally adjusted and propensity-score matched survival analysis. When taking into account unmeasured confounding by instrumental variable analysis, no differences in survival was found between the treatments for a selected group of patients. Further clinical studies are needed to

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

Page 7

characterize this group of patients, which can serve as a basis for future comparison studies for treatment recommendations.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The **South African National Clinical Trials Register** provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst CANSA has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.



Sources and References consulted or Utilised

Bodgi, L., Bahmad, H.F., Arail, T., Al Chobog, J., Bou-Gharios, J., Cheaito, K., Zeidan, Y.H., Eid, T., Geara, F. & Abou-Kheir, W. 2019. Assessing radiosensitivity of bladder cancer in vitro: a 2D vs 3D approach. *Front Oncol.* 2019 Mar 19;9:153. doi: 10.3389/fonc.2019.00153. eCollection 2019.

Canadian Cancer Society

http://www.cancer.ca/Canada-wide/About%20cancer/Types%20of%20cancer/Signs%20and%20symptoms%20of%20bladder%20cancer.aspx?sc_lang=en

Cancer Council Victoria

http://www.cancervic.org.au/about-cancer/cancer_types/bladder_cancer/treatment-for-bladder-cancer.html

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

Cancer.Net

<http://www.cancer.net/cancer-types/bladder-cancer/staging-and-grading>

Cancer Research Institute

<https://www.cancerresearch.org/we-are-cri/home/cancer-types/bladder-cancer>

Cancer Research UK

<http://www.cancerresearchuk.org/cancer-info/cancerstats/types/bladder/riskfactors/bladder-cancer-risk-factors>

<http://www.cancerresearchuk.org/cancer-help/type/bladder-cancer/about/types-of-bladder-cancer>

Cancer Treatment Centers of America

<http://www.cancercenter.com/bladder-cancer/bladder-cancer-risk-factors.cfm>

European Association of Urology

http://www.uroweb.org/fileadmin/user_upload/Guidelines/06%20Bladder%20Cancer.pdf

Female Urinary Tract

<http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001517/figure/A000486.B1122/?report=objectonly>

Flannery, K., Boyd, M., Black-Shinn, J., Robert, N., Kamat, A.M. 2019. Outcomes in patients with metastatic bladder cancer in the USA: a retrospective electronic medical record study. *Future Oncol.* 2019 Apr 3. doi: 10.2217/fon-2018-0654. [Epub ahead of print]

Genetic Reference

<http://ghr.nlm.nih.gov/condition/bladder-cancer>

Fuller, T.W., Acharya, A.P., Meyyappan, T., Yu, M., Bhaskar, G., Little, S.R. & Tarin, T.V. 2018. Comparison of bladder carcinogens in the urine of e-cigarette users versus non e-cigarette controls. *Sci Rep.* 2018 Jan 11;8(1):507. doi: 10.1038/s41598-017-19030-1. PMID: 29323232.

Ghate, K., Brennan, K., Karim, S., Siemens, D.R., Mackillop, W.J. & Booth, C.M. 2018. Concurrent chemoradiotherapy for bladder cancer: practice patterns and outcomes in the general population. *Radiother Oncol.* 2018 Jan 3. pii: S0167-8140(17)32764-0. doi: 10.1016/j.radonc.2017.12.009. [Epub ahead of print]. PMID: 29306498.

Häggström, C., Garmo, H., de Luna, X., Van Hemelrijck, M., Söderkvist, K., Aljabery, F., Ströck, V., Hosseini, A., Gårdmark, T., Malmström, P.U., Jahnson, S., Liedberg, F. & Holmberg, L. 2019.

Survival after radiotherapy versus radical cystectomy for primary muscle-invasive bladder cancer: A Swedish nationwide population-based cohort study. *Cancer Med.* 2019 Apr 1. doi: 10.1002/cam4.2126. [Epub ahead of print]

Kim, H.S., Kwak, C., Kim, H.H. & Ku, J.H. 2019. The cancer of the bladder risk assessment (COBRA) score for predicting cancer-specific survival after radical cystectomy for urothelial carcinoma of the bladder: external validation in a cohort of Korean patients. *Urol Concol.* 2019 Mar 29. pii: S1078-1439(19)30099-7. doi: 10.1016/j.urolonc.2019.03.006. [Epub ahead of print]

MacMillan Cancer Support

<http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Bladder/Bladdercancer.aspx>

Male Urinary Tract

<http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001517/figure/A000486.B1123/?report=objectonly>

Mao, W., Ma, B., Huang, X., Gu, S., Luo, M., Fan, J. & Geng, J. 2019. Which treatment is best for patients with AJCC stage IV bladder cancer? *Int Urol Nephrol.* 2019 Apr 4. doi: 10.1007/s11255-019-02105-5. [Epub ahead of print]

Medscape Reference

<http://emedicine.medscape.com/article/2006834-overview>

Memorial Sloan-Kettering Cancer Center

<http://www.mskcc.org/cancer-care/adult/bladder/diagnosis-treatment-msk>

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2019

Page 9

MD Anderson Cancer Center

<http://www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/bladder-cancer/index.html>

<http://www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/bladder-cancer/prevention/index.html>

PubMed Health

<http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001517/>

Renal & Urology News

http://www.renalandurologynews.com/bladder-cancer-obesity-link-confirmed/article/405908/?DCMP=EMC-RENALUROLOGY_TODAYSUPDATE&cpn=&hmSubId=&hmEmail=OdsiBxRYPdkldpZ00Ap-a5dX4uYlpfYu0&spMailingID=11028228&spUserID=MzMMyODk3NTcxNTcS1&spJobID=520047546&spReportId=NTIwMDQ3NTQ2S0

Shinagare, A.B., Ramaiya, N.H., Jagannathan, J.P., Fennessy, F.M., Taplin, M.E. & Van den Abbeele, A.D. 2011. Metastatic patterns of bladder cancer: correlation with the characteristics of the primary tumor. *AJR Am J Roentgenol.* 2011 Jan;196(1):117-22. doi: 10.2214/AJR.10.5036

Smith, A.B., Jaeger, B., Pinheiro, L.C., Edwards, L.J., Tan, H.J., Nielsen, M.E. & Reeve, B.B. 2018. Impact of bladder cancer on health-related quality of life. *BJU Int.* 2018 Apr;121(4):549-557. doi: 10.1111/bju.14047. Epub 2017 Nov 1.

TNM Classification Help

<http://cancerstaging.blogspot.com/2005/02/urinary-bladder.html>

Weill Cornell Medical College

<https://www.cornellurology.com/clinical-conditions/bladder-cancer/types-of-bladder-cancers/>

Winchester Hospital

<http://www.winchesterhospital.org/health-library/article?id=32653>

Zargar, H., Shah, J.B., van Rhijn, B.W., Daneshmand, S., Bivalacqua, T.J., Spiess, P.E., Black, P.C. & Kassouf, W. 2018. Neoadjuvant dose dense MVAC versus GC in patients with cT3-4aNOMO bladder cancer treated with radical cystectomy. *J Urol.* 2018 Jan 9. pii: S0022-5347(18)30036-3. doi: 10.1016/j.juro.2017.12.062. [Epub ahead of print]. PMID: 29329894.