General

Mental Health in Urologic Oncology

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This article is a systematic review of mental health in urologic oncology patients with prostate cancer (PCa), bladder cancer (BC), renal cell carcinoma (RCC), testicular cancer (TC), or penile cancer (PeCa). For all pathologies, a focus on increasing quality of life post-treatment demonstrated a positive impact in reducing Mental Health Illness (MHI) prevalence. Cancer specific mental health care may be given to patients to reduce suicide risk in BC patients and sexual identify and masculinity counseling may improve mental health for TC or PeCa patients. In order to better accommodate patient's mental health needs when undergoing GU cancer treatment, we recommend incorporation of mental health metrics such as questionnaires to assess early treatment of MHI, a greater emphasis on psychosocial support with the patient's loved ones, peers, and healthcare team, alongside advising healthy habits such as exercise which has been shown to drastically reduce MHI incidence across all pathologies. We hope that these measures conducted by urologists and oncologists, alongside possible coordination with psychiatrists and psychologists for psychotherapy, psychopharmacology, and neuro-stimulation treatment modems may be helpful in the long term to reduce MHI incidence in urology oncology patients. Given the higher incidence of MHI in oncology patients and in the patient population after the Covid-19 pandemic, MHI awareness in the sphere of urologic oncologic treatment continues to be crucial when creating a collaborative treatment platform for patients.

INTRODUCTION

Mental health is sometimes easy to overlook when treating physical conditions. It can be helpful for healthcare providers to account for mental health when providing treatment protocols. Mental health illness (MHI) has become more prevalent during the recent coronavirus 2019 (COVID-19) pandemic. One global cross-sectional study noted 50.9% of participants displaying anxiety traits whereas 58.6% exhibited depression whereas another meta-analysis study concluded that 25% of adults experienced significant stress due to the pandemic.[1,2] In light of this fact, major depressive disorder (MDD) prevalence has been estimated to be 13% (95% CI: 11-15%) or 16.3% (95% CI: 13-20%) for cancer patients as opposed to 4% in the general population.[3-5] Patients with malignancies have a significantly increased risk of suicide compared to the general population, even when accounting for precancer diagnosis psychiatric care use.[6] When patient's psychiatric needs are not met, treatment adherence for cancer patients can be negatively affected.[7]

This review article focuses on the care of urologic oncology patients. Oftentimes, treatment of chronic genitourinary (GU) malignancies is dictated by a complex boundary of diagnosis-therapeutic algorithms to maximize survival

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rates. However, side effects from treatment can oftentimes affect an individuals' well being and quality of life (QoL). Surgery can cause risks of life-long impotence or urinary incontinence and radiation can cause worsening obstructive symptoms.[8] Androgen deprivation treatment (ADT) was associated with increased risk of depression and cognitive impairment in prostate cancer patients.[9] As such, careful coordination with baseline assessments and recommendations are necessitated during treatment. In a study conducted in Ontario, Canada, patients with prostate cancer (hazard ratio (HR): 2.23; 95% CI: 1.69-2.94) and bladder cancer (HR: 2.18; 95% CI: 1.62-2.93) hospitalized for MHI before their cancer diagnosis had a higher likelihood of dying from their malignancy.[10] In another comparative study, there was a noted 60% increase in risk of suicidal death during the first 50 months of diagnosis, bladder cancer, given its higher mortality rate, were at a higher risk of suicide by patients upon diagnosis (HR: 1.73; 95% CI: 1.14-2.62) compared to prostate (HR: 1.07; 95% CI: 0.90-1.27) and kidney (HR: 1.26, 95% CI: 0.79-2.02) cancers.[6] A Surveillance, Epidemiology, and End Results database from 1988-2010 analysis concluded male sex was found to be associated with greater odds of suicide in bladder (odds ratio (OR): 6.63) and kidney cancer (OR: 4.98) patients. Increasing age was also associated with suicide for patients with prostate, bladder, and testis cancer (OR: 1.03-1.06).[11]

The objective of this paper is to provide an up-to-date overview of mental health studies, findings, complications, treatment modems conducted within the urologic oncology space including prostate cancer (PCa), bladder cancer (BC), renal cell carcinoma (RCC), testicular cancer (TC), and penile cancer (PeCa) pathologies. Given the higher incidence of MHI as an aftermath of both the Covid-19 pandemic and a cancer diagnosis, MHI awareness in the sphere of urologic oncologic treatment by healthcare providers becomes useful when creating a collaborative treatment plan for patients.

PROSTATE CANCER

EPIDEMIOLOGY

Prostate cancer (PCa) is the second most common cancer amongst men worldwide according to the WHO and the most common cancer amongst men in the United States with a lifetime incidence of 1 in 8 men.[12,13] Overall, with treatment in the United States, patients with PCa have a five year net survival rate of 99%, amongst the highest when compared to other cancer pathologies.[14] PCa incidence is strongly related to age, more common in men older than 65 years of age.[15] Per epidemiologic studies, African American men demonstrate higher rates of PCa compared to other ethnic groups.[16,17]

CLINICAL PRESENTATION/DIAGNOSIS

PCa in early stages is usually asymptomatic, however sometimes patients may have complaints of frequent urination, difficulty starting and maintaining a steady urinary stream, nocturia or dysuria.[18] There may also be issues with sexual function and performance such as difficulty achieving erection or ejaculation.[19] Metastatic PCa, namely to bones, can lead to severe bone pain oftentimes along the vertebrae, hips, ribs, or femur.[20] Prostate digital rectal exams (DRE) may detect abnormalities in structures such as hard nodules or asymmetry but it is not a definitive test.[21] Oftentimes, elevated prostate specific antigen (PSA) levels usually greater than 4ng/ml in the blood is how 80% of PCa present even though elevated levels can present when benign.[22,23] At least 2 abnormal PSA levels or the presence of a palpable nodule from the DRE are used as clinical criteria to justify further investigation. A biopsy is used as the diagnostic confirmatory tool for PCa, where imaging such as magnetic resonance imaging (MRI) has recently been employed as an adjunct.[22,23]

PATHOPHYSIOLOGY/RISK FACTORS

The prostate is a walnut-sized gland located between the bladder and the penis approximately 3 centimeters long weighing 20 grams.[24] It is located at the base of the penis of males, immediately anterior to the rectum, and surrounds the posterior part of the urethra.[24,25] The prostate gland is responsible for producing 30-35% of seminal fluid that nourishes sperm and provides alkalinity, requiring androgen for optimal function.[24]

PCa most commonly occurs in the peripheral basal prostate glandular cells.[26,27] As an adenocarcinoma, PCa cells multiply initially spreading to surrounding prostate tissue and may remain localized at the prostate for decades.[28] PCa may metastasize to bone and lymph nodes, partially due to prostatic venous plexus draining into the vertebral veins.[28]

PCa also has a strong genetic connection where males with family history of PCa and BRCA1/BRCA2 or MSH2/MSH6 mismatch repair gene germline pathogenic variants have a higher incidence of PCa.[29,30] A diet high in animal fat and low in vegetables has been shown to be associated to increased PCa, however alcohol and coffee consumption are not significant.[31-34] Pooled analysis of 18 prospective studies demonstrated that there was no association of PCa with sex hormone levels such as testosterone, dihydrotestosterone, and estrogen.[35]

TREATMENT OF MENTAL HEALTH COMPLICATIONS FOR PCA PATIENTS

As alluded to previously, GU malignancies can often be confounded with mental health variables due to the challenges that come with treatment protocols. PCa is not a stranger to this: 19.7% of a sample PCa population even before treatment demonstrated depressive symptoms.[36] In a large analytical sample including 25,183 men aged 45-85 years from the Canadian Longitudinal Study on Aging that measured mental health outcomes resulted that survivors of PCa compared to those without netted statistically significantly higher odds of psychological distress (aOR: 1.52, 95% CI: 1.09-2.11) and positive scores for depression (aOR: 1.24; 95% CI: 1.02-1.51).[37] In order to better understand treatment of mental health complications both pre- and

post- PCa treatment, this section will provide an overview on studies conducted on MHI over the course of various PCa treatment modems, then delve into the recommendations for treatments of MHI complications associated specifically with PCa patients based on the literature.

First, a 2014 study analyzed a total of 50,856 men, 65 years of age of older with clinically diagnosed PCa, taken from 1992-2005 Surveillance, Epidemiology, and End Results Medicare database to better understand the primary outcomes of MHI development in PCa patients.[38] The high-power study concluded that patients treated with "definitive" therapy such as a radical prostatectomy (RP) or radiation therapy (RT) netted lower risk of patients developing MHI.[38] Possible description for this phenomenon was patients undergoing active surveillance (AS) treatment may have lead to patients subconsciously feeling the cancer is not actively being treated and leading to negative mindset.[38] However, an expert column response published in 2016 to the 2014 study noted that the 2014 study was limited due to being restricted by age.39 They also noted contradicting studies finding no difference in anxiety levels between patients treated with RP and AS or anxiety levels after AS.[39,40] One of these studies was a cohort of 679 men which concluded that moderate or higher levels of depression and anxiety were low in men with localized PCa associated with sexual outcomes but was high in PCa cased associated with urinary outcomes.[39] The response concluded that provisions of early psychologic referral as an option for PCa treatment was indicated which we also agreed.[41] Understandably, the conclusion to be made is PCa treatment choice should be carefully coordinated between the urologist and the patient's diverse set of circumstances both physically and mentally for less MHI incidence. Ultimately, careful history taking and questioning during clinical presentations may assist providers in determining the next step on if patients may be indicated for MHI preventative resources.

Androgen deprivation therapy (ADT) has also recently become a topic of discussion for MHI specifically for PCa patients. In a retrospective observational cohort study of approximately 40,000 veterans with PCa treated with RT, an increase in risk of development of depression and use of outpatient psychiatric services was observed (HR: 1.50; 95% CI: 1.32-1.71 and HR: 1.21; 95% CI: 1.16-1.27 respectively).[42] Another study compared Beck Depression Inventory (BDI) scores 6-months after treatment initiation for ADT and RP where depressive symptoms were exacerbated in PCa patients undergoing ADT.[43]

A recent 2019 published study by Matta, et al. examined antidepressant prescription across men greater than 66 years of age after treatment of nonmetastatic PCa in Ontario, Canada from 2002 to 2019.[44] This study linked men who underwent RP (n=4952), RT (n=4994), or AS (n=2136), and matched them to the general population (n=57,127).[44] Through differences-in-differences analysis adjusted for demographic factors, the study found men had significantly increased odds of antidepressant receipt 5 years after RP (OR: 1.49; 95% CI: 1.35-1.64) or RT (OR: 1.33; 95% CI: 1.21-1.47) but did not have increased odds of antidepressants after AS (OR: 1.15; 95% CI: 0.94-1.41).[44] Possible reasons linked here were erectile dysfunction, low sexual desire, urinary incontinence for post-RP settings and loss of QoL domains for RT when combined with ADT; however, the authors also recognized the limitations that antidepressants did not necessary equate to MHI incidence and can be associated with the treatment of separate non-MHI associated conditions.[44] Understandably, a letter responding to this study by Kim and Chung was denoted discussing if invasive therapies do induce depression because of the unremitting urogenital side effects post-treatment.[45] The letter went on to conclude that while there was no hard data suggestive of this yet, inclinations of such conclusions could be possible.

We agree that through our literature search, besides the 2014 paper, many studies concluded a greater potential MHI incidence rate from RP, RT, and ADT as opposed to AS. For example, another cross sectional analysis of 632 male participants aged 36-69 from the 2009-2015 Atlantic PATH cohort survey, demonstrated that survivors of PCa post-surgery compared to other forms of cancer post-surgery in controlled analysis had a statistically significant higher odds of screening positive for depressive symptoms but not significant for anxiety symptoms.[46] As such, it may be the case that given the less recurrence rates of post-definitive operative treatment such as RP, the 2014 study was linking a greater likelihood for anxiety symptoms post-AS and that there would be a greater depression signs for patients post-RP, RT, or ADT. However, given that these studies are not conclusively hard evidence for causation, we agree with the recommendations made by Kim and Chung that a potential Antonovsky sense of coherence (SOC) scale in measuring coping and reflection skills to a person's measure of QoL can catch potential MHI development early post interventional treatments.[45] At the same time, when discussing different treatment options for PCa, decision-related distress for patients need to be taken into account. One prospective longitudinal study of 111 male participants denoted 63% had high-decision related stress, with the stress persisting in 42% of men 12 months post-treatment even with high satisfaction of treatment choice.[47] As such, careful coordination and connections between the physician and the patient should be taken into account when choosing the right PCa treatment for their circumstance. Whatever best treatment modem is chosen, patients need to be followed through detailed histories and questionnaires to assess for any mental health changes and catch early MHI incidence.

Lastly, one study measured the effects of a low-intensity telephone intervention by nurse counsellors giving five sessions (pre-treatment, 2, 6, 12, and 24 months post-treatment respectively) of psycho-education to reduce stress during treatment for Australian PCa patients.[48] Self-reported survey data on cancer specific distress, decision related distress, cognitive judgement, well being, and QoL measures were collected. Per this study, there were no unconditioned effects for the intervention and Chambers, et al. cited that individual heterogeneity may have been the reasoning for the results.[48] For example, according to the study, younger men with higher education and income im-

proved on indices for mental well-being while younger men with lower education did not experience mental health benefits.[48] Additionally, men who were older did not experience any mental health benefits, citing potential poorer sexual function before treatment leading to a lessened QoL domain effect post PCa treatment.[48] There were also couple other studies notating the benefits that physical activity and avoiding sedentary behavior has on mental health: one study discussed the benefits of physical activity for PCa patients undergoing ADT and another study reported that lower levels of aerobic exercise was associated with reduced physical and mental health for PCa patients with bone metastases.[49,50]

In conclusion, for PCa patients, we found a greater number of studies citing associations with mental health effects and incidence for MHI post-interventional treatment such as RP, RT, and ADT given QoL marker changes. However, one study noted on potential greater incidence for anxiety post AS. To better catch MHI incidence, implementing surveys such as SOC scales during history taking and throughout PCa management visits could be indicated as opposed to nursing education calls. Physical activity post-interventional PCa or during AS could be encouraged by the physician to reduce anxiety, depression, and stress. Careful coordination could be conducted between the healthcare team including psychotherapists and the patient to create the best treatment plan that fits the patient's unique physical health, mental health, and socioeconomic circumstances.

BLADDER CANCER

EPIDEMIOLOGY

Bladder cancer (BC) is the 10th ranked cancer in terms of prevalence across the globe. The United States ranks near the top of the list along with other well-developed countries. It is interesting to note that BC prevalence is to a degree positively correlated with how advanced a nation is in terms of the human development index (HDI) and gross domestic product (GDP) but this does not give us a complete picture.[51]

In a study analyzing the HDI for various genitourinary cancers to include BC, it was found that the mortality-to-incidence ratio (MIRs) was higher for a lower HDI nation compared to a higher HDI nation. Taken all together, it is of value to not only consider the economical layout of a nation, but also the mortality vs. morbidity rate; and the positive impact that psychiatric services can yield for urological oncology patients.[51,52]

CLINICAL PRESENTATION/DIAGNOSIS

BC is typically a slow onsetting cancer from the time of a patient's initial exposure. It is often caused by an inducing agent such as: tobacco, work environment, genetic inheritance, or from schistosomiasis depending on the geographical location.[51] Continually, considering the anatomy of the bladder and its function to store and excrete urine, it encounters many chemical agents which can be carcinogenic. One of the initial indications of BC is hematuria which can lead to use of computed tomography (CT) scans to determine if BC is indeed present.[51] Thankfully, about 70% of cases can be confirmed in the initial stages.[51]

PATHOPHYSIOLOGY/RISK FACTORS

Considering the structure and function of the bladder it is not surprising that the vast majority of BC cases are in the urothelial cells. These cells make the most superficial lining of the bladder and thus come into close contact with harmful agents. Continually, almost all BC cases are being diagnosed in patients who are at least 55 years old. This further implies that BC is slower progressing than other types of cancer and might not be present until years removed from a patient's initial exposure with a risk factor such as tobacco or an occupational hazard.[51]

TREATMENTS OF MENTAL HEALTH COMPLICATIONS OF PATIENTS WITH BC

With the diagnosis of BC, it is imperative to not only focus on the physical implications of the disease but the psychological impact and stress it can induce. In a nonsystematic study looking at a collection of available literature relating to BC and its implications relating to mental health, a total of 19 applicable publications were analyzed. It included 11 prospective studies and 8 retrospective studies. The study saw an association between depression and anxiety aligning with a worse prognosis for the patient.[53]

With a general understanding that BC can induce additional stress and burden on patients, it is imperative that patients are receiving the necessary mental support in conjunction with physical support. In a study focusing on the usage of a mental health care service (MHS), it was found from a population of just under 4300 patients treated for BC that patients who had previously established continuity with an MHS sought out MHS during and after treatment much more than patients without a prior relationship with an MHS. Of further interest was a statistically significant difference in seeking out MHS post-treatment for male patients compared to female patients.[54]

Another key variable to consider regarding BC is the specific patient population namely that the majority of BC patients are older individuals. This provides specific challenges for those diagnosed with BC when taking into conjunction patient's with pre-existing mental illness and how they are treated for the disease. Through a retrospective analysis of over 66,000 patients diagnosed with BC, it was found that approximately 6.7% of the patient population were previously listed as having a mental health disorder. The results demonstrated that patients with an underlying mental illness did not receive guideline-concordant treatment for the disease at a significant rate compared to patients without a previous mental illness thus resulting in a worse prognosis.[55] Continually, it was observed from a study of patients recently diagnosed with BC that the more demanding the treatment course was, the more instances of anxiety and depression occurred. They also discerned from their results that women had a higher incidence of anxiety and depression compared to men.[56]

A different study was conducted that analyzed the diagnosis of a psychiatric illness after muscle-invasive BC and the subsequent survival rates in elderly patients. It was found that the type of treatment used and being diagnosed with a psychiatric disorder played a significant role in the survival of the patient.[57] Patients who had a radical cystectomy compared to radiotherapy or chemotherapy showed a significantly higher risk of being diagnosed with a psychiatric disorder following treatment. In fact, the study concluded that over half of their sample population of 3709 patients ended up with a psychiatric diagnosis following BC treatment. Overall, the study displayed there could be a great need for further mental health treatments and interventions to help patients during the course of muscle-invasive BC.[57]

It is also important to consider the possibility of emphasizing a preventative approach to treating and managing mental illness in BC patients. In a study conducted with patients from Ontario, Canada, previous level of psychiatric intervention was assessed in patients prior to being diagnosed with cancer and subsequent cancer mortality and general mortality. A psychiatric utilization gradient (PUG) was formed with scores assigned to the level of psychiatric intervention namely 0: no intervention, up to 3: admitted to a hospital. The study included over 676,000 patients. The results showed a positive trend between the level of psychiatric intervention prior to diagnosis and the PUG and mortality of the patients from cancer and in general.[10]

In a study focused on understanding psychological wellbeing for patients with BC the Roy's Adaptation Model (RAD) was used.[58] RAD was used to analyze BC patient's wellbeing in conjunction with structural equation modelling. Some of the key variables studied were the patients age, length of time they had the disease, and gender to list a few. The results of the study showed numerous challenges that BC patients might face such as being male and being more advanced in age. The use of RAD and structural equation modelling in this study could help lead to a formalized intervention to better care for the mental health of BC patients but more research is needed.[58]

Continually, the psychological wellbeing of the BC patient could also relate to the confidence and understanding they have from their urologist. One study analyzed and discerned a correlation between the level of unease a patient had mentally in relation to how well informed they felt from their urologist regarding BC. Overall, the study pointed to the idea that urologists should strive to make sure their patients are well informed and clear on the severity of BC they are facing and an appropriate course of action moving forward.[59]

With an increased understanding and emphasis on the importance of mental health, not much has been centered on patients with urological cancers. In a literature review of over 15,000 records, it was distilled down to 10 studies fitting the criteria analyzing the feasibility and acceptance of interventions for mental health in urological cancer patients.[60] The 10 studies focused on patients with either prostate or kidney cancer leaving more room and further study for BC patients specifically. What was of interest is the patients who had symptoms of depression positively benefited from either group intervention or couples' intervention. Each type of intervention demonstrated a decrease in symptoms of depression, but the size of the data is a possible limiting factor and one to consider for additional research.[60] Furthermore, BC treatments have the potential to yield undesirable effects on patient's sexual organs and mental wellbeing. More research is needed to formalize quantifiable psychological metrics for patients' sexual health following BC treatment.[61]

A different study was conducted to analyze the effects of depression on tumor growth and severity of BC in mice. The main metrics measured were the size of the tumor after subjecting the mice to chronic unpredictable mild stress and several immune cells and molecules involved in the immune response. The results showed more immune cell inhibition in the subject group compared to the control. This led researchers to recommend addressing the importance of mental health in patients with BC with the displayed potential that it could help BC patients have a more favorable outcome.[62]

Overall, further research in the mental health in BC patients is recommended from our literature review. We were able to discern from numerous studies that key variables such as: a patient's previous mental health prior to BC diagnosis, gender, severity of BC, treatment plan, and confidence/clarity from their urologist in treating their BC all to a degree have an impact on the patient's mental health and following prognosis.

RENAL CELL CARCINOMA

EPIDEMIOLOGY

Renal Cell Carcinoma (RCC) is the leading variation of kidney cancer (KC). The prevalence of RCC varies considerably.[63] It is higher in North America and Europe as opposed to South America and Asia.[63] The incident rate also varies by gender with males typically having a higher rate. Continually, the incidence rate in the United States for developing RCC went from 10.6/100,000 to 12.4/100000 between 2001 and 2010 and has strong association with a patient's age.[63]

PATHOPHYSIOLOGY, RISK FACTORS, AND CLINICAL PRESENTATION

Some of the key risk factors pertaining to RCC include smoking, hypertension, and obesity. Furthermore, potential risk factors for RCC include: analgesics, diabetes, and trichloroethylene exposure.[64]

Of all the listed risk factors, cigarette smoking is one that is suggested to increase a patients' likelihood of getting RCC at a rate of 50% and 20% for male and female smokers respectively. The study also suggests that RCC is more likely to be diagnosed in smokers; this may be related to smoking causing chronic hypoxia in patients' tissue from carbon monoxide.[63]

In a study looking at the incidence, prevalence, and mortality rates of RCC across the world, a data collection from GLOBOCAN was used for assessment. The results of the

study showed great variation in these three variables across the globe.

RCC most of the time manifests as adenocarcinoma within renal parenchyma. There has been an uptick in the incident rate of RCC in the United States with the majority being at an earlier tumor progression stage for diagnosis.[63] RCC is often diagnosed incidentally from an increase in imaging procedures in the current practice and delivery of healthcare.[63,64] Continually, RCC instigates a worse prognosis and is more lethal than different urological diagnoses such as PCa, TC or PeCa.

MENTAL HEALTH IN PATIENTS WITH RCC/KC

With a diagnosis of RCC, it is expected to take a given toll on not only a patient's physical health but also mental health. In a study looking at different variables involved in RCC treatment and RCC patients' health related quality of life (HRQoL), a database search was conducted.[65] Several of the key variables examined were the method of treatment the patient underwent such as laparoscopic nephrectomy vs. open surgery and their proceeding physical wellbeing. In the laparoscopic group, patients showed significantly better physical health after surgery than the open surgery group. Despite a noted difference in physical wellbeing, mental health data between the two groups did not express a representable trend. Furthermore, the study found that a patients' HRQoL correlated more with how they viewed the renal function they did have. Ultimately, the study documented that notable HRQoL factors included: the size and stage of the tumor, patient's age, BMI, education, and job status.[65] They determined that further research and building a structure to better assess HRQoL variables in RCC patients was recommended. Furthermore, having representable and measurable HRQoL metrics could better assist the patient-provider relationship in delivering effective and efficient care to RCC patients.[65]

In a similar study assessing HRQoL outcomes in patients with KC, a longitudinal retrospective cohort study was performed. HRQoL was measured based on a mental component summary and physical component summary. It included data from 1998-2013 comparing KC patients with controls who did not have cancer.[66] Part of the aim of the study was to see long-term impacts on HRQoL in KC vs non-KC patients. The results of the study concluded that KC significantly impacted patients who made less income, had a later stage of KC, and were more advanced in years compared to other patients with KC.[66] This further reiterates the importance of obtaining representable and measurable HRQoL metrics to improve the patient-provider relationship.[65,66] Continually, it is beneficial to take into context not only RCC in patients, but other key contributing factors such as comorbidities in patients such as coronary artery disease and chronic kidney disease in a given patient. The treatment outcome expectations will likely be different in patients with multiple diseases and thus reemphasizes the importance of establishing quantifiable HRQoL metrics.[67]

Continuing off of the thought of different treatment approaches in patients with RCC, a study was conducted specifically on a population of Japanese patients. These patients underwent sunitinib treatment (chemotherapy) for RCC and the aim of the study was to see how sunitinib treatment impacted the HRQoL in the given patient population.[68] The results of the study do acknowledge the fact that the study was non-randomized and had a small sample size but there are still meaningful conclusions to draw upon. For instance, the results indicated that efficacy as opposed to adverse events might be connected to a higher HRQoL in the patients who underwent RCC treatment via sunitinib.[68]

Furthermore, a different study focused on three key psychological symptoms being depression, anxiety, and stress and if they were statistically significant in patients with KC.[69] The researchers performed a statistical analysis on 250 patients ranging in age from 25-76 with a predominantly male population totaling 73%. The results of the analysis noted that symptoms of anxiety, depression, and stress in patients were 91.2%, 87.2%, and 93.6% respectively.[69] The results indicated statistically significant differences among the gender, age, and income levels of the patients.[69] Ultimately, the results pointed to the importance of addressing mental health in KC patients based on the findings of depression, anxiety, and stress they exhibited.[69]

Further building upon the need to better address mental health in KC patients, a team of researchers analyzed psychological disorders and psychosocial resources for KC patients.[70] They completed a cross-sectional study with a patient population of 489.[70] They also performed a regression analysis looking at possible associations among psychosocial resources and psychological disorders. The results indicated that the rate of depression was 77.5% compared to a rate of 69.3% for patients with anxiety.[70] Ultimately, the study noted a significant association between a patient's perceived social support from their family and connection with depression and anxiety.[70]

Continuing on the importance of social support in KC patients, a study comparing perceived social support and depression between cancer survivors and patients without cancer was performed. The study expressed potential differences between KC patients and patients without cancer among these variables.[71] One key difference observed was that patients who had KC expressed more pain and dyspnea in conjunction with worse physical wellbeing.[71] On the flipside, KC survivors noted more perceived social support compared to the control group. Taken altogether, KC survivors and the control group displayed comparable HRQoL while KC survivors might have strengthened their perceived social support compared to the control group.[71]

TREATMENTS OF MENTAL HEALTH COMPLICATIONS OF PATIENTS WITH RCC

Considering the importance of mental health in patients, specifically with RCC, a study was conducted looking for potential links between KC and selective serotonin reuptake inhibitors (SSRI).[72] Through a retrospective cohort analysis, the researchers concluded that patients using SSRIs citalopram and paroxetine over a two-year induction

timeframe had a significantly lower risk towards RCC. Ultimately, researchers concluded that not only do citalopram and paroxetine appear to possibly lower the KC risk, but they can also serve their immediate function in addressing depressive symptoms in KC patients.[72]

In a different study analyzing the impact depression and anxiety had on the patients' survival following nephrectomy, a couple of conclusions were ascertained. Initially, they found that both depression and anxiety did not show statistical significance in relation to a KC patients' outcome from surgery.[73] Overall, the researchers alluded to the idea that more studies are recommended to better analyze the impact of depression and anxiety in KC patients.[73]

Another beneficial way to help KC patient's QoL was assessed looking at variables of self-efficacy and resiliency among KC patients and how these attributes impacted their QoL.[74] A cross-sectional study was implemented with 103 patients. The researchers concluded that KC patients who were not as depressed displayed higher self-efficacy and in conjunction more resiliency. For patients without depression, more resiliency and happiness seemed to yield a better QoL. Overall, the researchers pointed to the importance of providers addressing a given patient's emotional state and working to better their QoL with more resiliency and overall better self-efficacy.[74]

Thinking about the team effort involved in treating patients with KC, the quality of the patient-provider relationship as noted in the previous study examined can have a lasting impact on the QoL of a patient with KC. Furthermore, we should also consider addressing another key role in the treatment and overall outcome for a patient with KC being their caregivers. Caregivers play a notable role for KC patients, but they can also face significant mental health obstacles of their own. In a study to examine the level of anxiety and depression a caregiver might face, it was found that their "experiences of care" and "information needs" appeared to be related to higher anxiety and depression.[75] They also discerned that the amount of time spent as a caregiver, stage of KC, and experiences of care throughout KC treatment had a negative impact on the caregivers' anxiety and depression. In summary, the study points to the importance of considering the whole team involved in a patient's treatment for KC. Being able to better address the mental health needs of each member could positively impact the prognosis in KC patients and mental health of the teammates involved.[75]

Continually, the type of cancer and approach to treatment can also factor in for a patient's mental health. A study was performed to look at the level of psychological challenges cancer patients might face prior to surgical intervention. They noted that previous studies suggest that not even 50% of cancer patients are diagnosed and thus appropriately treated for depression and anxiety.[76] This is an alarming statistic as previous studies point to the implications that adverse mental health can have on HRQoL in KC patients and other types of cancer. The researchers did a cross-sectional study design to analyze depression and anxiety levels in a sample of 207 patients. Despite previous studies implications on the percent of cancer patients not receiving appropriate intervention for anxiety and depression, their results were lower comparatively. Furthermore, tumor type, sex, and type of surgery had a significant correlation to worse mental health. Additionally, patients who were either female, had a kidney tumor, or received radical nephrectomy displayed elevated anxiety levels.[76]

In summary, further studies should be performed to not only address mental health challenges in RCC patients, but also the importance of positive relationships for all involved parties. This might potentially benefit not only the RCC patient's mental wellbeing and survival, but cultivate stronger relationships and HRQoL among patients, providers, and caregivers.

TESTICULAR CANCER

EPIDEMIOLOGY

Testicular cancer (TC) is rare cancer that represents about 1% of cancers in men overall, but is the most common cancer in males between the ages of 15 and 35 years with an excellent greater than 95% survival rate.[13,77] In the United States, nearly 10,000 males will be diagnosed with TC each year with fewer than 500 deaths annually.[78]

Interestingly, the incidence of TC has been increasing in the world over the past 30 years based on a combination of complex factors—the exact causes of increased TC incidence are unclear.[77]

CLINICAL PRESENTATION/DIAGNOSIS

Upon physical examination, TC can present as a firm, painless mass as well as dull or aching pain in the scrotum and/or testes, with or without painless swelling and redness.[79] Additionally, about 5% of patients with TC can present with symptoms of metastasis such as gynecomastia, lumbar back pain, bone pain, or a neck mass.[79]

Scrotal ultrasonography and CT imaging for any suspected metastases in other body structures is required, and ultrasound can usually detect if masses are extra- or intratesticular.[80]

PATHOPHYSIOLOGY/RISK FACTORS

The most common risk factors of TC include cryptorchidism (or undescended testicles), gynecomastia, family history of TC, genetic disorders such as Klinefelter and Down syndrome, infertility, and germ cell neoplasia.[81-87]

TREATMENTS OF MENTAL HEALTH COMPLICATIONS OF PATIENTS WITH TC

The psychological aspects associated with diagnosis of TC and subsequent surgical treatment are well-characterized. Anxiety and depressive conditions and symptoms along with increased body image issues have been seen to affect sexual function in TC survivors.[88,89] Specifically, TC patients are seen to have depression and anxiety at 19% and 13.5% higher rates than the general population, respectively.[90]

It is important to note that within TC patient groups, males who only received an orchidectomy (surgical resection of one or both testicles) reported minimal impact to their mental health compared to those who had chemotherapy or radiotherapy as part of their cancer treatment regimen.[91] Chemotherapy and radiotherapy are known to have associated toxicities such as nausea and vomiting, neurotoxicity, cardiovascular and metabolic diseases, sexual (ejaculatory) dysfunction, among others that can lead to anxiety, depression, and decreased QoL.[90,92] Indeed, it is reported that TC patients have a higher prevalence of anxiety and depressive disorders during chemotherapy (40% and 14.6%, respectively) than after treatment (18.5% and 9.3%, respectively).[93]

Although it could be thought that time after TC diagnosis and treatment could alter QoL, it was found that time since cancer diagnosis had no association with QoL.[94] In addition, among all TC survivor groups, there was also a fear of losing fertility (although untrue) as well as a fear of reoccurrence that negatively affected QoL and self-esteem.[89,91,95] Interestingly, it is also noted that TC survivors have a higher incidence of negative health behaviors including poor diet of inadequate fruits and vegetables, increased body-mass index, inadequate exercise, risky alcohol consumption, and smoking.[96]

The treatment options for mental health complications in TC patients are diverse, however, some may suggest treatment of immediate anxiety and depressive symptoms with medications. Findings show that TC patients who possess significant adverse health outcomes after cisplatin-based chemotherapy (such as hearing impairment, peripheral sensory neuropathy, and kidney disease) are significantly more likely to use anxiolytic and antidepressant medications, as they are safe and effective to use in TC patients.[97-99] These findings may suggest the debilitating effects of chemotherapy toxicities on survivors' mental health and their attempts to mitigate the effects pharmacologically.

Most notably, it was also found that TC patients who engage in strenuous physical activity are less likely to use pharmacologic interventions.[97] Indeed, some studies go further to show that vigorous exercise can be used to mitigate treatment-related depression and HRQoL with physical, psychological, social, and spiritual components.[100] One analysis suggests that the rate of depression in physically active TC survivors (9%) was significantly lower than survivors who were inactive (17%).[101] Another randomized control trial reports that high-intensity interval training significantly improved fatigue, self-esteem, and HRQoL.[102] Conversely, there are conflicting studies that show there is no significant effect of vigorous physical activity on mental health conditions such as anxiety and depression.[102,103] Based on the varied findings, additional randomized control trials are needed to determine the effect of strenuous physical activity on mental health conditions in TC patients.

Furthermore, additional mental health support from partners or caregivers are seen to help TC patients cope during and after treatment. It is shown that survivors with a relationship at diagnosis and after TC treatment had more satisfaction with support, higher self-esteem and mental health, as well as better physical and emotional coping to the disease than survivors who were single.[104,105] While good partner and caregiver support can alleviate the risk of lower mental health, additional studies are needed to determine the effect of psychological service usage and therapists on mental health complications. Particularly in Canada, it is known that TC survivors have a substantially higher rate than baseline mental health service users of visiting primary care physicians for mental health concerns such as anxiety during the 2-month peri-treatment and post-treatment periods.[106] However, there is a distinction between usage and benefit, as well as its generalizability to places outside of Canada.

In our review, diagnosis and treatment of TC can often bring on various psychological morbidities, made worse by toxicities arising from increasing amounts of chemotherapy. Although more robust data is needed to draw a clear relationship between strenuous exercise or mental health service utilization on psychological conditions, staying active and having adequate support through relationships with partners, caregivers, and physicians is promising to reduce mental health complications in patients with TC.

PENILE CANCER

EPIDEMIOLOGY

Penile cancer (PeCa) is a rare malignancy with a prevalence of 0.1-1 cases per 100,000 men in well-developed European countries and the United States.[107] In contrast, PeCa has a prevalence of up to 7 cases per 100,000 men and accounts for up to 17% of male cancers in under-developed parts of South America, Africa, and Asia.[107]

In the United States, PeCa has an average incidence rate of 0.81 cases per 100,000 men and only accounts for less than 1% of male malignancies with fewer than 500 deaths each year.[13,108] While most PeCa diagnoses are between 50-70 years of age, males of any age can be affected and incidence rates increase with age.[108]

CLINICAL PRESENTATION/DIAGNOSIS

The most common signs of PeCa upon physical exam are painless nodules on the glans, ulcerations on the foreskin, and inguinal lymphadenopathy.[109,110] To differentiate between inflammatory (psoriasis, lichen planus, angiokeratomas), infectious (genital herpes, primary syphilis), and pre-malignant or malignant penile lesion presentations, biopsy of the primary lesion and/or suspected enlarged inguinal lymph nodes for histological analysis is necessary and crucial.[110]

Of all malignant penile lesions, approximately 95% are squamous cell carcinoma with the remaining being diagnosed as basal cell carcinoma, Kaposi sarcoma, melanoma, and lymphoma, among others.[111]

PATHOPHYSIOLOGY/RISK FACTORS

The most common risk factors of PeCa include human papillomavirus infection, human immunodeficiency virus infection, obesity, phimosis associated with a lack of circumcision, smoking, lack of hygiene, and ultraviolet-A phototherapy for genital psoriasis.[112-117] In addition, medical conditions such as genital warts, urinary tract infections, penile tearing, and penile injury are associated with an increased risk of PeCa.[117]

TREATMENTS OF MENTAL HEALTH COMPLICATIONS OF PATIENTS WITH PECA

A diagnosis of PeCa is usually associated with subsequent surgical resection of malignant lesions along the penis, which could result in partial or total removal of the penis and altered penile sensation and function. Consequently, men after PeCa surgery have reported changes such as diminished sexual and urinary function, anxiety, depression, and alterations of body image and sexuality.[118-126]

Multiple studies have shown that changes in appearance of the penis after surgery can diminish self-esteem and a sense of masculinity.[120,127] Because the penis is an integral part of a man's identity and sexuality, PeCa patients with significant penis tissue removal after surgery could consider reconstructive surgery to restore appearance, function, and build back self-esteem. In fact, it has been shown that PeCa patients who underwent reconstructive penis-sparing surgery had preserved penile appearance, maintained urinary and sexual function, and favorable HRQoL assessment scores.[128]

As reconstructive surgery is not an option for all PeCa patients, mental health resources are extremely important to combat psychological and psychosexual morbidities. Surprise at the impact of surgery and subsequent shame post-procedure can be mitigated through open discussion with supportive peers and therapists.[120] Sharing experiences with positive thinking (joy and humor) in a group discussion setting with other post-surgical PeCa patients has been seen to facilitate men's feelings and increase confidence as well as empowerment of self.[120] Having a sexual health therapist is another form of support for PeCa patients to provide solutions and advice for facilitating pleasurable sex with their partners.[120]

In our review, there is no standardized treatment plan for post-surgical PeCa patients due to diverse outcomes and individual differences. However, because the penis is crucial to a man's sexuality and identity in interpersonal relationships, a combination of genital-sparing procedures with psychological support from peers or therapists can have a positive impact on a patient's mental health and post-operative outcomes.

CONCLUSION

Patients with advanced GU malignancies report greater prevalence of psychosocial distress, including suicidal risk, alongside lessened QoL post-treatments.[129] From the review of the diverse set of GU cancer treatment, we also understand that there is great difference in MHI needs depending on the pathology. For PCa, given its more promising survival rates and common occurrences, we understand that MHI incidence should be monitored, especially regarding QoL changes post-interventional treatment such as RP, RT, and ADT. Psychosocial surveys conducted during the treatment protocol alongside advising for physical activity may help in reducing the anxiety and stress during management. For BC, we recognize the greater mortality rate can lead to greater odds of suicidal ideation especially among elderly patients.[6] As such, careful coordination between psychosocial specialists concentrating on suicidal management may be worth greater emphasis for BC patients with MHI. While mortality for RCC is not as high as BC, the less promising prognosis compared to other urologic pathologies calls for a focus of mental health treatment in conjunction to improving HRQoL. Furthermore, RCC/KC literature on mental health netted a greater focus of attention on improving social support of both patients and caregivers. For rarer malignancies with better prognosis such as TC and PeCa, sexual identity, masculinity, and fertility becomes the focus of bridging mental health concerns post-operatively. Psychological support from peers, therapists, and healthcare providers alongside balancing exercise during the post-operative recovery were found to greatly reduce the incidences of MHI.

Given findings of MHI and suicide risk within urologic oncology, it could be helpful for physicians and healthcare providers in urology to coordinate between medical, socioeconomic, and psychosocial factors in treatment for urogenital cancers.[130] This is especially true for patients of low socioeconomic or racially underrepresented backgrounds who may not have said access to mental health resources during treatment of urogenital cancers.[131]

To provide greater psychosocial support for patients undergoing GU cancer treatment, incorporating mental health metrics into patient care (such as questionnaires to assess early treatment for MHI) and a combined effort of careful coordination with psychiatrists and psychologists for psychotherapy, psychopharmacology, and neuro-stimulation treatment modems may be helpful.[132,133]

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