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REVIEW

Sarcopenia in Urinary Bladder Cancer: Definition, Prevalence and Prognostic Value in Survival

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ABSTRACT

Sarcopenia, defined as the systemic loss of muscle function and mass, is commonly seen in advanced oncologic states, usually in conjunction with cancer cachexia. Bladder cancer represents one of the most common neoplasms worldwide and affects mainly the elderly who are already frail. The purpose of this study is to review the potential association between sarcopenia and bladder cancer in patients receiving different types of treatments. A thorough MEDLINE/PubMed non-systematic literature review was conducted from 1990 to January 2022, using the following search terms: "sarcopenia and bladder cancer" and "low muscle mass and bladder cancer". Sarcopenia probably poses a negative impact on the prognosis of patients at any stage of bladder cancer, as it is linked with overall worse survival, cancer specific survival and progression-free survival in those treated, with either radical cystectomy or chemotherapy. In addition, sarcopenia seems to be a strong predictor concerning complications and a negative prognostic factor following chemotherapy and surgery for bladder cancer. On the other hand, it seems that sarcopenic patients who receive radiotherapy or immunotherapy are not so severely affected.

Keywords: sarcopenia, overall survival, bladder cancer, complications, radical cystectomy

INTRODUCTION

Sarcopenia was first described by Irwin Rosenberg in 1989 and reflects the decrease of muscle mass due to aging (1). Decrease in muscle mass has been directly related to loss of independence, reduction of strength and falls (2). According to the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia is the co-occurrence of low muscle mass and function, while the loss of muscle mass with preserved muscle function is defined as "pre-sarcopenia" (3). Even if strength is considered to be a stronger predictor of sarcopenia compared with lean muscle mass, it falls under subjective errors in measurement (1). Bladder cancer is the tenth most common form of cancer worldwide, accounting for 3% of global diagnoses and being four times more common in men than women

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(4). In 2020, 81 400 new cases were diagnosed and 17 980 bladder cancer related deaths were recorded only in the USA (5). The purpose of this non-systematic review is to explore the potential interplay between these two entities.

Bladder cancer

The most common histologic subtype of bladder cancer is derived from transitional bladder epithelium, forming urothelial carcinomas (4). Smoking is considered the main etiology of bladder cancer (4). This neoplasm is commonly seen in those who work in petroleum and aniline dyes industries (4). Hematuria is a common symptom before diagnosis being set by ultrasound, computed tomography (CT) or cystoscopy (4). Bladder cancer is categorized to non-muscle invasive (NMIBC) and muscle-invasive (MIBC) disease based on the histology after the first diagnostic transurethral resection of the bladder (TURB). This categorization is important, since the two subtypes are treated differently and associated with variable prognosis (4). The treatment for NMIBC consists of transurethral resection of the bladder tumor, followed by intravesical instillations of immunotherapy or chemotherapeutic agents, depending on the cancer stage and patient's baseline profile (4). Radical cystectomy with urinary diversion and pelvic lymphadenectomy is considered the gold standard for the treatment of MIBC and high grade NMIBC. This treatment can be followed by neoadjuvant chemotherapy. The five-year survival rates following this procedure are nearly 60% (1, 4). However, in case of metastatic disease, overall survival in most patients does not overpass 15 months despite systemic chemotherapy (4). There is encouraging data that innovative systemic immunotherapy may shift this paradigm (4).

The concept of sarcopenia

Sarcopenia is a degenerative and systemic loss of skeletal muscle, ranging from 15-50% in patients older than 65 years (4, 6). Genes such as myostatin gene (MSTN), vitamin D receptor (VDR) and angiotensin converting enzyme (ACE) are associated with body muscle-distribution phenotype (4). Sarcopenia is usually associated with lower physical activity and thus with metabolic syndrome, insulin resistance and cardiovascular system diseases (4).

Sarcopenia can be present due to advanced age (primary) or lack of exercise, cancer, poor nutritional status, endocrine or other systemic and inflammatory diseases (secondary) (1, 7). Inflammation, which is mediated by inflammatory and pro-inflammatory cytokines, can stimulate tumor cell proliferation as well as protein degradation and myofiber apoptosis. Inflammatory processes, along with oxidative stress, are also mediated by excessive fatty acid oxidation and lead to increased muscle wasting (4, 6, 8, 9).

There are several methods to assess sarcopenia. The most common method is the use of validated tools such as "Strength, Assistance with Walking, Rise from a Chair, Climb Stairs and Falls" (SARC-F) score, the "Short Portable Sarcopenia Measure" (SPSM) and the "Perioperative Nutrition Screen" (PONS) (10). Methods to quantify sarcopenia include dual energy X ray absorptiometry, bioelectrical impedance, ultrasound, magnetic resonance imaging (MRI) and CT (10); the latter provides an objective measurement of muscle mass with 1.4% precision error (1). Some authors report the use of skeletal muscle index, *i.e.*, the total skeletal muscle mass area adjusted for patient height or psoas muscle index, *i.e.*, the total psoas muscle area again adjusted for height (1). Adjustment of height values is necessary for males (11). In skeletal muscle index sarcopenia is diagnosed as low muscle mass at the third lumbar vertebra (L3) (1). Another metric is skeletal muscle density measured in Hounsfield units (1, 4). Several muscles can be used for sarcopenia assessment, including the psoas, paraspinal, transverse abdominal, external oblique or internal oblique and rectus abdominis muscle (2). The most current cut off values of sarcopenia are defined by Martin *et al* (2). A main drawback of these clinical metrics is the incorporation of single muscle measurements, which cannot be a true representative of total muscle area in cancer patients (11). While the general population with a higher BMI have a high skeletal muscle mass, some people with "sarcopenia obesity" or myosteatosis characterized by excessive infiltration from adipose tissue and low lean muscle density (1, 8). This condition promotes systemic inflammation and insulin resistance (1). Myosteatosis increasingly gains popularity over sarcopenia as a preoperative marker in cancers of the gastrointestinal tract as well as pancreatic and ovarian cancer (8).

Because sarcopenia is significant and can adversely affect cancer prognosis, it would be wise to try and prevent or even reverse it. Ritch *et al* claim that perioperative oral nutrition can prevent sarcopenia, post-radical cystectomy complications and lower readmission rates. Evidence suggests that malnourished individuals should be adequately fed enterally or even parenterally for at least 7-10 days preoperatively, in order to increase protein synthesis and limit degradation with a protein rich diet (12). Anabolic effects of diet are dramatically enhanced by physical exercise, particularly in the form of anaerobic exercise and resistance training (10). Anabolic agents such as testosterone, estrogens and growth factors can also be used (2, 4).

Immunonutrition consists of diets rich in nutrients such as glutamine, arginine, omega-3 fatty acids and ribonucleic acids, which halt inflammation and promote protein anabolism (13). Medications such as actin related protein 2 b inhibitors (ActR2b) block skeletal muscle protein degradation, acting on ActR2b, a receptor for myostatin and activin A with studies showing skeletal muscle hypertrophy in mice (4). Drugs against insulin resistance and inhibitors of lipolysis are commonly employed in reversing the effects of sarcopenia (4). Hormone replacement therapy is commonly used in menopausal associated sarcopenia (4). Novel pharmaceutical agents such as magnolol, flucoidan and anamorelin are currently undergoing investigation for their effects in cachectic patients (14).

The enhanced recovery after surgery (ERAS) protocol has proven to be effective in lowering postoperative complications and shortening the hospital stay (6, 12). Discontinuation of smoking and excessive alcohol consumption is considered of paramount importance (15).

Literature review

In this non-systematic review, PubMed and MEDLINE databases were thoroughly searched from 1990 to January of 2022, using "bladder cancer" AND "sarcopenia" OR "decreased muscle mass" as key terms, and were independently screened by one author and rechecked by other two authors. Any potential disputes were solved by a fourth author.

From the screened studies, the original ones were used in order to conduct the investigation of the potential interplay between these two entities, as shown in Table 1. Some systematic reviews were included in this article, because they contained definitions necessary for the present review. Studies using animal models were excluded.

Association between sarcopenia and bladder cancer

Radical cystectomy (RC) is a major surgery with high complication rates and major changes in body image, patient functionality and independence (16).

Frailty is thought to lead to greater susceptibility to physical stress such as surgery. This is caused by the depletion of body physical reserves. Frailty can also encompass cognitive and psychosocial changes associated with many conditions (17). According to a recent medical consensus, frailty is defined as "a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death" (18). Malnourished patients can be identified at the presence of two of the following criteria: inadequate food intake, weight loss, loss of subcutaneous tissue (fat or muscle mass), fluid accumulation and lower functional status (18). Malnutrition is prevalent in 14-55% of radical cystectomy patients (18).

Poor nutritional status together, catabolism and systemic inflammation commonly seen in terminally ill oncologic patients, especially in elderly and those with low exercise level, are linked with poor prognosis and lead to sarcopenia (4, 6, 8).

Phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt) signaling pathway, which regulates muscle mass homeostasis, is thought to be the key regulator for the metabolic pathway of sarcopenia and cachexia (19).

Smith *et al* came to the conclusion that complications following RC were independent of sarcopenia ($p=0.26$), but when the results were divided for both sexes, a striking increase in major complications was observed in sarcopenic women, as 43% of them used to experience complications compared to 10% of non-sarcopenic ($p<0.01$) (20).

Mayr *et al* state that sarcopenia is an independent predictor of both 90-day mortality

(OR 2.59; 95% CI 1.13-5.95; p=0.025) and major complications, especially CD 4a-5 (p=0.003) (21). The incidence of grade 3 or higher complications according to the Clavien-Dindo system ranges between 5-26% (21). Gao *et al* reported that sarcopenia was an independent predictor of venous thromboembolism (VTE) in patients undergoing RC (10.6% *vs* 1.8%; p= 0.005) (22). Maeda *et al* state that male sarcopenic patients, especially those with psoas muscle index (PMI) <400 (p=0.02), have a greater length of hospitalization following surgery (p=0.04) and lower overall survival, (23). However, muscle loss alone due to sarcopenia does not explain the increased rate of complications. Some factors that enhance the adverse perioperative outcome include the muscle denervation due to aging and mitochondrial dysfunction, with both playing a role in muscle strength and function (24). Moreover, the effects of body mass index (BMI) on postoperative morbidity and mortality are unclear, most probably due to several definitions of sarcopenia and the need to distinguish obesity with low *vs* obesity with high lean muscle mass. According to Psutka *et al*, no obesity related five-year overall survival (OS) benefit was noted after stratifying patients based on sarcopenia (p=0.2-0.7), while initial evidence pointed that increased BMI was correlated with a better OS (p=0.03) (25). According to Yamashita *et al*, sarcopenia (p<0.01) and myosteatosis (p=0.04) are associated with poor overall survival (8). Kwon *et al* concluded that obese and overweight patients had a better prognosis, as showed by recurrence free survival

TABLE 1. Studies concerning the potential interplay between sarcopenia and bladder cancer

Authors (Ref)	Year/study	Study population	Findings	Sarcopenia assessed by
Smith *et al* (20)	2013/retrospective	224 patients following radical cystectomy	Negative association between sarcopenia and major complications in women	TPA as assessed by CT
Mayr *et al* (21)	2018/retrospective	327 patients following radical cystectomy	Negative association between sarcopenia and 90-day postoperative complications	Lumbar skeletal muscle mass index by CT
Stangl-Kremser *et al* (46)	2018/retrospective	94 patients treated with TURBT and radiotherapy for UBC	High prevalence of sarcopenia in patients with bladder cancer. Not prognostic of survival	SMI according to Martins criteria, BMI to assess for sarcopenic obesity
Saitoh-Maeda *et al* (23)	2017/retrospective	78 patients following RC	Negative association between hospitalization, OS and sarcopenia in male sarcopenic patients	PMI as measured by CT normalized to height
Wang *et al* (28)	2021/retrospective	112 patients with UBC following RC	Negative association between high AGS, low TPI in OS and DFS. CTAs predictive value for therapy	TPI, AGS, CTA
Wang *et al* (30)	2019/retrospective	285 patients with UBC	No association between modifiable risk factors and sarcopenia	SMI at L3 level
Mayr *et al* (2)	2018/multicenter retrospective	500 patients following RC	Negative association between sarcopenia and five-year OS and CSS. Sarcopenia independent predictor of CSS and all-cause mortality	Lumbar SMI
Psutka *et al* (25)	2014/retrospective	262 patients with UCB treated with RC	No association between ACM and adiposity or obesity in sarcopenic patients	FMI, SMI, BMI
Psutka *et al* (31)	2014/retrospective	205 patients with UCB treated with RC	Negative association between ACM, CSS and sarcopenia. Sarcopenia associated with increased CSS and ACM	Lumbar SMI
Ha *et al* (32)	2019/retrospective	80 patients with UCB treated with RC	Sarcopenia independent predictor of OS	Lumbar SMI
Taguchi *et al* (34)	2015/retrospective	100 patients with metastatic UCB	Sarcopenia an independent predictor of poor CSS	TPA, lumbar SMI, U-TPT, TPT
Shimizu *et al* (35)	2022/retrospective	240 patients with UCB treated with chemotherapy	Negative association between sarcopenia and OS	TPI, paraspinal SMI and total SMI
Stangl-Kremser *et al* (42)	2018/retrospective	30 patients with UCB who received upfront cisplatin-based chemotherapy before RC	No association between pre-NAC sarcopenia and response to therapy	L3 SMI
Lyon *et al* (39)	2019/retrospective	183 patients with UCB who received NAC before RC	Negative association between post treatment sarcopenia and CSM	L3 SMI
Zargar *et al* (43)	2017/retrospective	60 patients with UCB who were treated with NAC and RC	No association between PMV changes and response to chemotherapy, postoperative complications or survival	PMV

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Kasahara *et al* (44)	2017/retrospective	27 patients who received gemcitabine and nedaplatin chemotherapy for advanced UBC	Sarcopenia is a negative predictor of OS	PMI
Fukushima *et al* (4)	2020/retrospective	28 patients with advanced UBC treated with pembrolizumab	Lower ORR and PFS in sarcopenic patients	SMI of two consecutive muscle groups by CT
Ferini *et al* (47)	2021/retrospective	28 patients who received radiotherapy for advanced UBC	No association between OS, CSS and sarcopenia	L3 lumbar SMI
Almarzouq *et al* (48)	2021/retrospective	141 patients with MIBC treated with tetramodal therapy	No association between OS, response to therapy and sarcopenia	Lumbar SMI
Tanaka *et al* (49)	2020/retrospective	154 patients with MIBC treated with tetramodal therapy	No association between DFS, CSS and sarcopenia. Higher complication rates in non-sarcopenic patients	Lumbar SMI
Gao *et al* (22)	2021/retrospective	252 UBC patients following RC	Sarcopenia an independent predictor of VTE	L3 lumbar SMI
Hirasawa *et al* (33)	2016/retrospective	136 who underwent RC	Sarcopenia independent predictor of worse prognosis	Lumbar SMI
Yamashita *et al* (8)	2021/retrospective	123 patients following RC	Sarcopenia and myosteatosis independent predictor of poor CSS	L3 lumbar SMI
Stangl- Kremser *et al* (29)	2021/retrospective	441 patients with UCB who underwent RC	Sarcopenia is predictive of early complications	L4 TPI
Cohen *et al* (41)	2021/retrospective	91 patients with UBC treated with NAC and RC	Sarcopenia is predictive of high rates of complications post RC	L4 PMI
Martini *et al* (51)	2021/retrospective	70 patients treated with immune checkpoint inhibitors for advanced UC	High risk patients, *i.e.* sarcopenic patients shorter OS, PFS and lower chance of clinical benefit	Measurement of body composition risk score which includes lumbar SMI and VFI
Rimar *et al* (40)	2018/retrospective	26 patients with MIBC who received platinum based chemotherapy	Decrease in lean muscle mass and increase in sarcopenic patients following chemotherapy	L3 SMI
Regnier *et al* (45)	2021/retrospective	82 patients treated with NAC and RC	Changes in sarcopenic status during NAC. Sarcopenia associated with risk of postoperative complications	Lumbar SMI
Kwon *et al* (26)	2014/retrospective	714 patients who underwent RC	Overweight and obesity is associated with favorable OS and pathological features	BMI used only

TPA: total psoas area; CT: computed tomography; TURBT: transurethral resection of the bladder tumor; UBC: urothelial bladder cancer; SMI: skeletal muscle index; BMI: body mass Index; RC: radical cystectomy; OS: overall survival; PMI: psoas muscle index; AGS: albumin globulin score; TPI: total psoas index; DFS: disease free survival; CTA: skeletal muscle measurement, combination of AGS and TPI; L3: 3rd lumbar vertebral body; CSS: cancer specific survival; ACM: all-cause mortality; FMI: fat muscle index; TPA: total psoas area; (U)-TPT: transversal psoas thickness (at umbilicus); CSM: cancer specific mortality; NAC: neoadjuvant chemotherapy; PMV: psoas muscle volume; PMI: psoas muscle index; PFS: progression free survival; MIBC: muscle invasive bladder cancer; VTE: venous thromboembolism; L4: 4th lumbar vertebral body; VFI: visceral fat index.

(RFS) (obese *vs* normal: P<0.001; overweight *vs* normal: p=0.008) and cancer specific survival (CSS) (obese *vs* normal: p<0.001; overweight *vs* normal: p=0.019) following RC (26).

Nomograms for bladder cancer have been developed incorporating predictors such as biomarkers of systemic inflammatory response, lymph node status and sarcopenia for predicting non-confined disease status, lymph node involvement and OS, but they either lack external validation or include small sample sizes (27). Wang *et al* concluded that albumin and globulin scores were related to TNM stage and could be a strong predictor of OS and DFS (28). In this study, Wang *et al* reported that a high AGR was associated with greater OS (p=0.036) and better DFS (p=0.016) (28). The same applies for high total psoas index (TPI) and survival rates (p=0.045 and 0.049, respectively) (28). The combination of TPI and albumin globulin score seems to be good predictor of OS and CSS following radical cystectomy (28). Stang-Kriemser *et al* proved that sarcopenia could predict early

complications following RC (HR 0.95; 95% CI 0.92-0.99; p=0.02) (29).

Studies tried to show the extent to which non-modifiable risk factors, modifiable risk factors and cancer-related factors can affect sarcopenia in bladder cancer (24). According to Wang *et al*, modifiable risk factors such as diet (p=0.822), physical activity (p=0.830) and individual nutritional components (p=0.259-0.983) are not associated with skeletal muscle indices in patients with urothelial bladder cancer (UBC) (30). According to Mayr *et al*, sarcopenia is an independent predictor of CSS (HR1.42; 95% CI 1.09-1.87; p=0.01) and all-cause mortality (ACM) (HR 1.42; 95% CI 1.00-2.02; p=0.048) in bladder cancer patients treated with RC (2). Five-year OS was lower in sarcopenic patients (38.3%) compared to non-sarcopenic ones (50.5%; p=0.002) following radical cystectomy (2). The same applies for five-year CSS (49.5% *vs* 62.3%; p=0.016) (2). Psutka *et al* demonstrated that sarcopenia was unfavorable for five-year OS (39% *vs* 70%; p=0.07) in non-sarcopenic patients and for ACM (49% *vs* 72%; p=0.03) in those with bladder cancer treated with radical cystectomy (31). Moreover, this study exhibited that sarcopenia was independently associated with an increased CSS (HR 2.14; p=0.07) and ACM (HR 1.93; p=0.04) (31). Similarly, Ha *et al* concluded that the decrease of muscle mass after radical cystectomy could be a negative prognostic factor in OS (p=0.012), with skeletal muscle index (SMI) decrease being an independent predictor for OS (HR 2.68; CI 1.007-7.719; p=0.048) (32). Hirasawa *et al* proved that sarcopenia was an independent predictor of unfavorable prognosis (HR 2.3; p=0.015), as showed by CSS of patients who underwent RC (33).

Taguchi *et al* stated that sarcopenia is also connected with diminished CSS in patients with metastatic urothelial carcinoma (HR 2.07; 95% CI 1.01-4.67) (34).

Shimizu *et al* pointed that sarcopenia leads to shorter survival rates, since OS was significantly longer in the non-sarcopenic study group (p=0.001) (35).

Radical cystectomy is associated with a wide range of perioperative and postoperative complications (4, 36). Radical cystectomy impairs gut motility and electrolyte balance partly due to bowel reconstruction, leading to significant weight loss, unmitigated protein wasting and increased fatty acid oxidation (10, 37). In case of neoadjuvant chemotherapy, the catabolic effects of the latter are added upon the already exhausting effects of surgical stress (38).

Sarcopenia is associated with increased cancer specific mortality after neoadjuvant chemotherapy according to Lyon *et al* (HR 1.90; 95% CI 1.02-3.56; p=0.04) (39). Sarcopenia after neoadjuvant chemotherapy (NAC) ranges between 2.6-6.4%, as measured in skeletal muscle indices (39). Rimar *et al* came to similar conclusions, with sarcopenic patients increasing after NAC from 69% to 81% (p=0.002) (40). Cohen *et al* stated that change in SMI after neoadjuvant chemotherapy (NAC) was associated with a higher rate of surgical complications following RC (HR 0.31; 95% CI 0.12-0.72; p=0.039) (41). However, according to Stangl-Kremser *et al*, if sarcopenia is present before initiation of chemotherapy, there is no clear association with the proportion of response to chemotherapy (p=0.16-0.65) (42).

In contrast, Zargar *et al* showed that there was no association between BMI, psoas muscle volume (PMV) changes and OS in patients treated with neoadjuvant chemotherapy and surgery (HR 1.01; 95% CI 0.95-1.08; p=0.74) (43). Kasahara *et al* described the prognostic significance of sarcopenia in patients receiving gemcitabine and nedaplatin based chemotherapy, which negatively affected OS (p=0.015) (223 days *vs* 561 days in the non-sarcopenic group) (44). According to Regnier *et al*, sarcopenic patients have an increased preponderance of early (HR 4.08; 95 CI 1.06-15.6; p=0.04) and late (HR 8.05; 95 CI 0.96-66.9; p=0.053) postoperative complications following NAC and RC (45).

According to Stangl-Kremser *et al*, there is no association between sarcopenia and either OS (HR 1.36; 95% CI 0.7-2.5; p=0.32) or CSS (HR 5.0; 95% CI 1.4-16.7; p=0.34) in patients treated with radiotherapy and transurethral resection of bladder tumor (TURBT) for advanced bladder cancer (46). Similar results were reported by Ferini *et al* in patients treated only with curative radiotherapy, with no substantial differences in the sarcopenic and non-sarcopenic groups (median OS 15 *vs* 42 months, respectively) (47). In patients who underwent trimodal therapy, no association was detected between sarcopenia and response to therapy or OS

(p=0.22-0.49), as reported by Almarzoup *et al* (48). According to Tanaka *et al*, in those treated with tetramodal therapy, *i.e.*, trimodal therapy plus partial cystectomy and lymph node dissection, there was no association between sarcopenia and survival rates being evident in five-year muscle invasive bladder cancer related regression free survival (MIBC-RFS) (97% and 97%, respectively, p=0.96) and CSS (94% and 94%, respectively; p=0.96) between sarcopenic and non-sarcopenic patients (49). In contrast to previous knowledge, complication rates were higher in non-sarcopenic patients than in those with established sarcopenia (22% *vs* 46%; p=0.02) (49). According to Fukushima *et al*, in patients undergoing immunotherapy it was demonstrated that sarcopenic ones had a lower response to therapy (21 *vs* 67% in non-sarcopenic patients (p=0.019) and lower progression free survival (PFS) (3 *vs* 15 months in non-sarcopenic patients; p=0.038) (50). According to Martini *et al*, sarcopenic patients receiving immune checkpoint inhibitors (ICI) for advanced urothelial cancer have a shorter OS (HR 6.72; p<0.001), shorter PFS (HR 5.82; p<0.001) and a lower chance of clinical results (HR 0.02; p=0.003) (51). ❑

DISCUSSION

From this non-systematic review, we concluded that sarcopenia was a bad prognostic factor for patients following RC, as it leads to increased 90-day mortality, ACM and complications, as well as decreased five-year OS and CSS. Some authors claim that an increased BMI has better prognosis in patients post-RC, as showed by their increased OS and CSS. This does not apply when an increased BMI is associated with sarcopenic obesity. Patients with metastatic UBC have poorer prognosis when the disease is associated with sarcopenia.

Neoadjuvant chemotherapy can lead to a decrease in muscle mass. Post-NAC sarcopenia can lead to higher complication rates following RC, while pre-NAC sarcopenia is not associated with patient's response to chemotherapy. Patients receiving systemic chemotherapy have a lower OS.

In the radiotherapy group, no significant differences between sarcopenic and non-sarcopenic patients were found. The same applies for patients who underwent trimodal or tetramodal therapy for UBC. In the group treated with immunotherapy, sarcopenic patients were less responsive to therapy with lower PFS.

Most of the studies included in this systematic review have a small sample number. Furthermore, they include a heterogeneous population and different tools of sarcopenia quantification, usually stemming from different definitions of sarcopenia. All studies were observational, retrospective and non-randomised. All the aforementioned factors necessitate the implementation of a larger multicenter randomized survey that uses a measurement of SMI derived from more than one muscle groups and encompasses the muscle strength as a criterion in the definition of sarcopenia. ❑

CONCLUSION

Sarcopenia seems to have a negative impact on the prognosis of bladder cancer patients at any stage, as it seems to have a negative impact on OS, CSS and PFS both in those treated with radical cystectomy and chemotherapy. In addition, it seems to be associated with increased complication rates postoperatively. Recovery of skeletal muscle mass and reversal of sarcopenia should be sought with administration of several available options; however, more studies are needed to further explore the value of each of these interventions. Perhaps nutritional and physical support as well as a multidisciplinary approach could be the best strategy. ❑

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