Bioelectrical Impedance Vector Pattern and Biomarkers of Physical Functioning of Prostate Cancer Survivors in Rehabilitation

Alexander Stäuber[1] (iD), Marc Heydenreich[2], Peter R Wright[3], Steffen Großmann[1], Niklas Grusdat[1], Dirk-Henrik Zermann[2,4] and Henry Schulz[1]

[1]Professorship of Sports Medicine/Sports Biology, Chemnitz University of Technology, Chemnitz, Germany. [2]Division of Sports and Training Science, Vogtland-Klinik Bad Elster, Bad Elster, Germany. [3]Department of Sport, Health Sciences and Social Work, Oxford Brookes University, Oxford, UK. [4]Department of Urology & Urooncology, Vogtland-Klinik Bad Elster, Bad Elster, Germany.

ABSTRACT

BACKGROUND: Knowledge of clinically established factors of physical function such as body composition, bioelectrical phase angle (PhA) and handgrip strength (HGS) with mortality predictive and health-related relevance is limited in prostate cancer survivors (PCS). Therefore, the aim of this study was to characterise and compare body composition data of PCS with extensive reference data as well as to analyse PhA and HGS and the prevalence of critical prognostic values at an early stage of cancer survivorship.

METHODS: One hundred and forty-eight PCS were examined at the start (T1) and end (T2) of a 3-week hospitalised urooncological rehabilitation, which began median 28 days after acute cancer therapy. Examinations included a bioimpedance analysis and HGS test. Comparison of body composition between PCS and reference data was performed using bioimpedance vector analysis (BIVA).

RESULTS: BIVA of the whole PCS group showed abnormal physiology with a cachectic state and a state of overhydration/oedema, without significant changes between T1 and T2. The age- and BMI-stratified subgroup analysis showed that PCS aged 60 years and older had this abnormal pattern compared to the reference population. HGS (T1: 38.7 ± 8.9 vs T2: 40.8 ± 9.4, kg), but not PhA (T1/T2: 5.2 ± 0.7, °), changed significantly between T1 and T2. Values below a critical threshold reflecting a potentially higher risk of mortality and impaired function were found for PhA in 20% (T1) and 22% (T2) of PCS and in 41% (T1) and 29% (T2) for HGS.

CONCLUSIONS: BIVA pattern and the prevalence of critically low HGS and PhA values illustrate the necessity for intensive continuation of rehabilitation and survivorship care especially in these 'at risk' cases. The routine assessment of body composition, PhA and HGS offer the opportunity to conduct a risk stratification for PCS and could help personalising and optimising treatment in rehabilitation and ongoing survivorship care.

KEYWORDS: Prostate cancer, BIVA, phase angle, physical function, rehabilitation, survivorship

Background

Prostate cancer is the most common solid organ cancer in men, with the highest incidence rates recorded in the developed countries of Oceania, North America and Europe.[1,2] With a focus on mortality, prostate cancer is the fifth leading cause of death from cancer in men.[2] Despite the high incidence, prognosis and survival rates are good.[3] However, there are well-known side-effects of prostate cancer therapy like urinary incontinence, erectile dysfunction, secondary lymphoedema, loss of muscle strength, muscle mass and bone mineral density[4-7] which finally lead to a deterioration of physical functioning. There is evidence that cancer patients with reduced physical function have a shorter life expectancy.[8-10] However, every prostate cancer survivor (PCS) in Germany is entitled to take part in a 3-week hospitalised urooncological rehabilitation

programme subsequent to acute cancer therapy which is the starting point of a longer-term survivorship care pathway for PCS. Beside coping with the disease, the treatment of disease- and therapy-associated functional limitations and psychological consequences as well as the improvement of reduced physical functioning and health-related quality of life are important rehabilitation goals.[11]

In view of parameters of physical functioning handgrip strength (HGS) has been identified as a strong biomarker and also a powerful predictor of mortality.[12-15] Body composition is also known as an important factor in physical functioning. Recently, the use of the raw impedance parameters resistance (R), reactance (Xc) and especially the phase angle (PhA) of bioimpedance analysis (BIA) has gained scientific attention.[16] These measures provide valuable information about the

hydration status, body cell mass and cell membrane integrity without algorithm-inherent errors associated with the conventional BIA approach, a common scientific method for predicting body composition. The bioimpedance parameter PhA, which also has been shown to be of prognostic value (eg, mortality, disease progression, incidence of post-operative complications), can be interpreted as a global marker of health status and as a biomarker of physical function.[16,17] Both are relevant components in the context of recovery, rehabilitation and general health outcome in cancer survivorship. However, the bioelectrical impedance vector analysis (BIVA), a method developed by Piccoli et al.,[18] enables a more detailed understanding of body composition compared to PhA alone.[16] BIVA uses the plot of raw impedance data R and Xc normalised per height (H) as a bivariate vector in a RXc vector graph. For instance, a lower R leads to a shortening of the vector and thereby reflects an excess of fluid, such as occurs in the case of oedema. In contrast, a reduced hydration status and dehydration causes a longer vector. High or low Xc indicates an increase or decrease of dielectric mass (membranes and tissue interfaces) of soft tissues, which causes the vector to move up or down. Based on the calculation of PhA from Xc and R, different vector locations in the RXc graph can theoretically be shown with comparable PhA. For this reason, the use of bioimpedance PhA alone is limited in terms of a clear differentiation between athletic (high phase angle, long vector) and obese (high phase angle, short vector) as well as lean (normal phase angle, long vector) and cachectic (low phase angle, long vector) subjects. Longitudinal changes in body cell mass and hydration status can be interpreted much better with the BIVA than with PhA, which makes the BIVA a valuable tool for body composition assessment and monitoring of PCS. In the clinical context, the BIVA method has significant advantages over the conventional BIA approach because no algorithms for conversion of raw impedance data into body-composition compartments are required. Results are therefore not biassed by the choice of regression equation, the accuracy of the criterion method or the selection criteria of the reference population.[19] Nowadays, BIVA is a widely used technique in medicine in different clinical conditions such as sarcopenia and sarcopenic obesity,[20] heart failure,[21] diabetes,[22] renal disease,[23] obesity,[24] COPD,[25] anorexia nervosa[26] and cancer.[27-31] Due to existing reference data in healthy populations for BIVA,[32] PhA[19] and HGS,[14] measures can be interpreted and classified in terms of their clinical relevance. For example, bioimpedance values within BIVA that fall outside the 75% tolerance ellipse of the reference population indicate an abnormal physiological situation[32,33] and a standardised PhA that falls below the fifth reference percentile appears to be a simple and prognostic relevant cut-off point for impaired functional and nutritional status and increased mortality.[10]

To date, however, no scientific data are available on BIVA, PhA and the prevalence of critical prognostic values of physical functional status of PCS in urooncological rehabilitation,

reflecting an early stage in cancer survivorship. The first aim of this study was therefore to characterise and compare BIVA data from PCS at the start (T1) and the end (T2) of a 3-week hospitalised urooncological rehabilitation programme with extensive reference data. The second aim was to evaluate PhA, HGS and the prevalence of critical prognostic values in these biomarkers of physical function at T1 and T2.

Methods

Participants and procedures

This observational study with repeated measures was conducted within the Rehabilitation Hospital Vogtland-Klinik Bad Elster, Germany. Between March 2017 and March 2019 a total of 175 PCS were recruited within the research project 'Return', which was approved by the ethics committee of Chemnitz University of Technology (V-182-17-AS-Tumor-20012017) and registered at the German Clinical Trials Register (ID: DRKS00014263). All participating PCS gave their written informed consent and fulfilled the inclusion criteria – diagnosis of prostate cancer, no defibrillator or cardiac pacemaker and no orthopaedic restrictions for execution of tetrapolar BIA and HGS assessment. All PCS were evaluated at the start (T1) and the end (T2) of a hospitalised 3-week urooncological rehabilitation programme, which constitutes the standard inpatient cancer rehabilitation duration in Germany[34] before being referred to a community-based rehabilitation programme. The median time interval between admission to hospital for urooncological rehabilitation and the end of acute cancer therapy (surgery, radiotherapy, chemotherapy) was 28 days.

The standardised examination procedure at T1 and T2 began with a single tetrapolar BIA measurement of R and Xc (BIA 5 series multifrequency, EgoFit GmbH, Germany) taken on the subject's right side between the right wrist and ankle in the supine position (after 10 minutes of supine rest) on a non-conductive surface at a fixed frequency of 50 kHz. Adhesive solid gel electrodes (Ambu® WhiteSensor 0315M, Denmark) were applied to defined anatomical sites on the dorsal surfaces of the hand, wrist, ankle and foot according to the manufacturer's instructions as follows: the proximal edge of the wrist electrode was applied on an imaginary line at the styloid process of the ulna and the distal edge of the finger electrode was applied on an imaginary line from the centre of the metacarpophalangeal joints of the middle and index finger. The proximal edge of the ankle joint electrode was placed along a imaginary line through the highest points of the outer and inner ankle bones. The distal edge of the toe electrode was placed along an imaginary line through the middle of the metatarsophalangeal joints of the second and third toes. PhA of BIA was calculated by using the following equation:

$$PhA\left[°\right] = \arctan\left(\frac{Xc}{R}\right) x(\frac{180}{\pi}) .^{16}$$

The HGS test was conducted following the standardised Southampton protocol.[35] Each participant was seated

comfortably in a standard chair without arm support, and with their hips flexed at 90° and feet resting on the floor. The elbow of the test arm was flexed to 90°, the forearm and wrist in neutral position, thumb facing upwards. Before the test, the hydraulic hand dynamometer (Baseline®, HIRes™, Gauge ER™, USA) was adjusted to the participant's hand size so that the device was comfortable in the hand. The examiner supported the base of the dynamometer for testing. Following a demonstration of the protocol, the participant was asked to squeeze the handle with as much force as possible for 3 seconds. Three repeated trials were recorded for both hands with a rest period of at least 15 seconds between trials. The starting hand was chosen randomly with subsequent side-alternating measurements. Only the peak value of HGS assessment was used for statistical analysis. Only PCS with complete measurement data were included in the final analysis.

Data analysis

The statistical analyses were conducted using IBM SPSS statistics 26 (Chicago, IL, USA). Statistical group comparisons between T1 and T2 were performed with Student's paired *t*-test. The effect size was calculated directly from the *t*-value and the number of participants using the formula: $Cohens' d_Z = t / \sqrt{N}$.[36] The significance level for all tests was set at $P < .05$.

BIVA was conducted with BIVA software (Piccoli A & Pastori G, Department of Medical and Surgical Sciences, University of Padova, Padova, Italy, 2002; available by E-mail: apiccoli@unipd.it). According to the RXc graph method,[18] measurement data of R and Xc were standardised by the height (H) of PCS and expressed in Ω/m. Confidence ellipses for PCS were calculated for the total group as well as body mass index (BMI) and age-specific subgroups using the BIVA software, whereas the calculation procedure of the confidence ellipses is explained in detail by Piccoli et al.[18,32] Confidence ellipses describe the area in which the 2-dimensional vectors fall within a 95% probability.[18] This implies that graphically non-overlapping 95% confidence ellipses are significantly different from each other ($P < .05$; which is equivalent to a significant Hotelling's T^2 test).[18] Because of a large sample size, the corresponding representativity and the comparability of the measurement principle, we used the tetrapolar BIA measurement data (model 1990B, operating at 50-kHz frequency; Valhalla Scientific, San Diego, CA, USA) of N = 1572 non-Hispanic white men of the United States collected in the Third National Health and Nutrition Examination Survey (NHANES III)[32] as reference population for all BIVA data analysis regarding PCS. Data of the bioimpedance vector components, PhA and HGS of PCS stratified by BMI and age can be found in Supplemental Table S1. Due to the lack of reference values for the BMI class >35 kg/m², N = 11 PCS could not be considered in the BMI subgroup analysis.

The prognostically relevant fifth PhA reference percentile, identified by Norman et al.,[10] served as a cut-off for detection of PCS at risk for impaired function and survival. In view of HGS the extensive normative data published by Steiber[14] were used as the chosen reference data in this study. Steiber[14] suggested a threshold to define a critically weak HGS associated with an increased mortality risk at values that lie ≥1 standard deviation below the standardised mean HGS. This threshold was also used in the present study to identify PCS with a potential elevated mortality risk.

Results

One hundred and forty-eight PCS were fully assessed at T1 and T2. Table 1 shows the baseline demographics and clinical characteristics.

Bioelectrical impedance vector analysis

The statistical comparison of raw impedance parameters and raw impedance parameters normalised for height at T1 and T2 is displayed in Table 2. Significant differences were found for R and R/H (both $P < .05$), whereas the effect size was small.

Figure 1 shows the BIVA RXc graphs with 95% confidence ellipses for the total group and the age- and BMI-stratified subgroups of PCS in relation to the reference impedance vector with 50%, 75% and 95% tolerance ellipses. At T1 and T2 the total group of PCS presented a mean impedance vector with 95% confidence ellipses located outside the 95% tolerance ellipse in the cachectic quadrant and a state of overhydration/oedema. Based on the graphical overlapping, no significant difference was detected between T1 and T2. For reasons of clarity and because of no noteworthy graphical or statistical differences of the age- and BMI-stratified BIVA graphs between T1 and T2 data are only presented for T1. With focus on the different subgroups the BIVA RXc graphs show significant differences between PCS and the reference population (Figure 1). No significant differences could be found in PCS between the different age groups. PCS from the age of 60 years and above with BMI of 19 to 25 kg/m² or >25 to 30 kg/m² were located outside the 75% tolerance ellipse in the cachectic quadrant and a state of over-hydration/oedema. All age groups of PCS with BMI >30 to 35 kg/m² showed an impedance vector position outside the 75% tolerance ellipse.

Biomarkers for physical function

Data of PhA and handgrip strength are presented in Table 3.

Between T1 and T2 a significant improvement, with a small effect size, was obtained for handgrip strength ($P < .001$) but not for PhA. Small to medium correlations were found between PhA and handgrip strength at T1 ($r = .41$, $P < .001$) and T2 ($r = .23$, $P < .01$). In 20% to 22% of PCS a critical PhA was detected at T1 and T2. At T1, 41% of PCS presented a critical

Table 1. Baseline demographics and clinical characteristics of N = 148 prostate cancer survivors in urooncological rehabilitation.

Age (years), mean (SD)	66.5 (7.4)
Height (m), mean (SD)	1.76 (0.07)
Weight (kg), mean (SD)	85.9 (16.2)
BMI (kg/m², mean (SD)	27.8 (4.8)
Cancer stage (UICC I-IV), N (%)	I = 35 (23.6), II = 63 (42.6), III = 32 (21.6), IV = 15 (10.1), n.a. = 3 (2.0)
Radical prostatectomy, N (%)	Yes = 124 (83.8), No = 24 (16.2)
Androgen deprivation therapy, N (%)	Yes = 17 (11.5), No = 131 (88.5)
Radiotherapy, N (%)	Yes = 35 (23.6), No = 113 (76.4)
Chemotherapy, N (%)	Yes = 6 (4.1), No = 142 (95.9)
Urinary incontinence, N (%)	Yes = 100 (67.6), No = 48 (32.4)
Coronary artery disease, N (%)	Yes = 14 (9.5), No = 134 (90.5)
Arterial hypertension, N (%)	Yes = 81 (54.7), No = 67 (45.3)
Type 2 diabetes mellitus, N (%)	Yes = 17 (11.5), No = 131 (88.5)

Abbreviations: n.a., data not available; SD, standard deviation.

Table 2. Raw data of bioimpedance analysis of prostate cancer survivors in urooncological rehabilitation.

| BIA DATA	T1 (N = 148)	T2 (N = 148)	*P*-VALUE	EFFECT SIZE
R 50 kHz (Ω)	448.8 (56.9)	453.2 (59.8)	.012	Cohen's d_z = .21
R/H (Ω/m)	255.8 (34.7)	258.3 (36.5)	.011	Cohen's d_z = .21
Xc 50 kHz (Ω)	40.6 (7.2)	40.9 (7.6)	.334	–
Xc/H (Ω/m)	23.2 (4.3)	23.3 (4.6)	.312	–

Abbreviations: *H*, height; *PhA*, phase angle; *R*, resistance; *T1*, start of rehabilitation; *T2*, end of rehabilitation; *Xc*, reactance.
Bioimpedance values presented as mean (standard deviation).

handgrip strength, which decreased to 29% at T2. Thirteen percent of PCS showed a combination of both critical conditions (PhA and handgrip strength) at T1 which decreased to 9% at T2.

Discussion

In the present study, for the first-time, PCS were examined with regard to their BIVA pattern and PhA in the early stage of cancer survivorship. Our main findings provide evidence that BIVA data of PCS in inpatient urooncological rehabilitation differ significantly from population-based reference data, with no statistical significance (within-group) change over time. Independently of the BMI BIVA values of PCS from the age of 60 years felt outside the BIVA reference ellipse of 75% (indicating an abnormal physiology), whereas the mean vector was situated in the cachectic quadrant (low body cell mass) and a state of fluid overload (apparent oedema). These findings can be explained by several factors. Firstly, prostate cancer specific treatments like radical prostatectomy, radiation therapy and androgen deprivation therapy (ADT) may cause

secondary lymphoedema. Secondly, many of the PCS in the present study suffered from comorbidities from the cardiovascular system (eg, arterial hypertension in 55% of PCS), which necessitate the use of potentially oedema-causing drugs. For instance, 22% of PCS took calcium channel blockers (eg, Amlodipine) which are used to treat high blood pressure and cause oedema by increasing capillary filtration of fluid and may reduce lymphatic drainage.[37] The lack of a statistically relevant change in the RXc graph over time could possibly be explained by the short duration of the rehabilitation hospital stay, which is probably too short for corresponding adaptations of the fluid load or dielectric mass of soft tissues. In view of this, various studies showed a change in the R and Xc values with respect to PhA after 12 weeks of progressive resistance training in older woman.[38,39] However, in order to avoid postoperative complications due to the short time difference of approx. 1 month between surgery (radical prostatectomy in 84%) and onset of rehabilitation, the majority of global muscle strengthening exercises as part of the medical exercise therapy in 3-week urooncological rehabilitation can only be carried
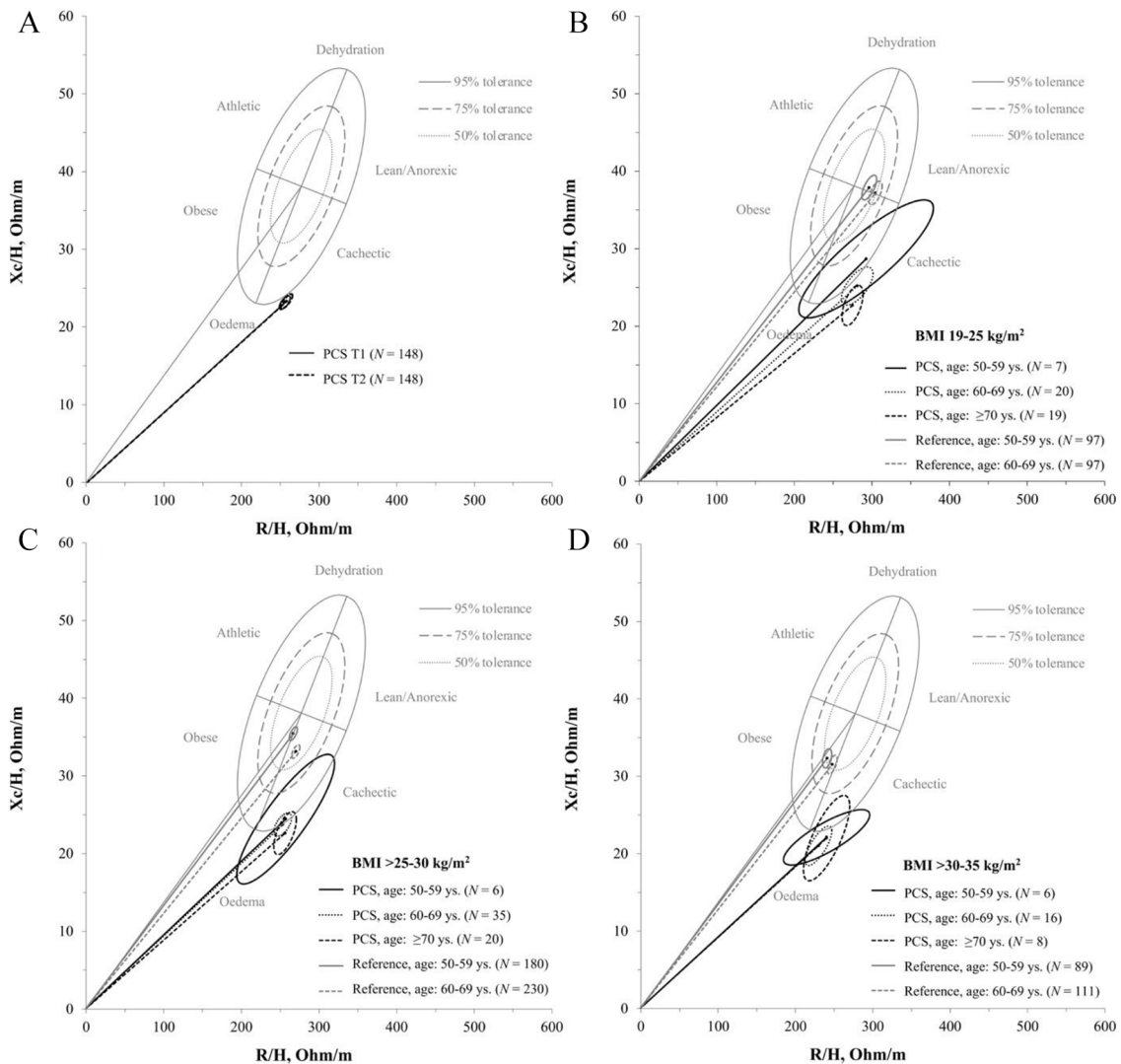
Figure 1. The BIVA RXc graphs of (A) the total group of prostate cancer survivors (PCS) at the start (T1) and the end (T2) of urooncological rehabilitation, (B) PCS with BMI 19 to 25 kg/m² stratified by age, (C) PCS with BMI >25 to 30 kg/m² stratified by age and (D) PCS with BMI >30 to 35 kg/m² stratified by age. All reference graphs are based on data of Piccoli et al[32] with sex-specific 50%, 75% and 95% tolerance ellipses (grey). Optimal body composition is located at the centre (within 50% and 75% tolerance ellipses). Bioimpedance values that fall outside the 75% tolerance ellipse of the reference population indicate an abnormal physiological situation.
Abbreviations: *H*, height; *R*, resistance; *Xc*, reactance.

Table 3. Biomarkers of physical function of prostate cancer survivors in urooncological rehabilitation.

	T1 (N = 148)	T2 (N = 148)	*P*-VALUE	EFFECT SIZE
PhA 50 kHz (°)	5.18 (0.70)	5.16 (0.66)	.469	–
Cases with critical PhA, N (%)	Yes = 30 (20.3) No = 118 (79.7)	Yes = 32 (21.6) No = 116 (78.4)	–	–
HGS (kg)	38.7 (8.9)	40.8 (9.4)	.000	Cohen's d_z = .40
Cases with critical HGS, N (%)	Yes = 60 (40.5) No = 88 (59.5)	Yes = 43 (29.1) No = 105 (70.9)	–	–

Abbreviations: *HGS*, handgrip strength; *PhA*, phase angle; *T1*, start of rehabilitation; *T2*, end of rehabilitation.
Phase angle and handgrip strength data presented as mean (standard deviation).

out with a low load. Ongoing ADT may also have contributed to this. In this context, a meta-analysis by Chen et al.[40] provided evidence that low- to moderate-intensity resistance and aerobic training is effective for improvement of muscle strength but may not be sufficient for affecting muscle mass.

Another reason could be the chronic use of medication with oedema-causing effects (eg, calcium channel blockers, non-steroidal anti-inflammatory drugs, corticosteroids, antidepressants) which maintained the oedema state during the rehabilitation phase.

PCS in the present study showed a mean PhA of 5.2° at the start and the end of the 3-week urooncological rehabilitation whereas a fifth of PCS presented a value below the fifth percentile of sex-, age- and BMI-stratified PhA reference values published by Bosy-Westphal et al.[19] Norman et al.[10] found that patients with a solid or haematological tumour disease which showed a PhA below the fifth reference percentile exhibited a significantly higher 6-month mortality risk (OR: 4.0; 95% CI: 2.4, 6.8; $P < .001$) and a 37.4% probability of death. Referring to the data of Bosy-Westphal et al.,[19] PhA in healthy adults usually range between 5° and 7° on average, depending on their age and BMI. Barbosa-Silva et al.[41] presented population-specific PhA reference values for men above 6°. In summary, PCS in the present study on average demonstrated a PhA at the lower spectrum of available reference values which reflects lower cellularity, cell membrane integrity and poorer cell function. However, further research is needed to evaluate if the PhA could also be increased in PCS by longer term rehabilitation interventions in survivorship care (eg, strength training). Further studies should also focus on PhA as a potential prognostic indicator for an increased mortality risk in PCS, especially in those with an identified PhA below the fifth reference percentile.

In addition, PCS showed a significant improvement of HGS after rehabilitation, albeit the effect size was small. Referring to the threshold for critically weak HGS obtained by Steiber,[14] two fifths of PCS presented critical values at the beginning of inpatient rehabilitation. After completion, critical values were still present in almost a third of PCS. Based on survival analysis, Steiber[14] showed that men whose HGS fell below the critical threshold had an 86% greater risk of death within 8 years of the HGS test. Besides these findings numerous other studies consistently confirm that low HGS increases the risk for mortality.[12,13,15] When considering the mean age of PCS in our study (66.5 years), the found HGS on average was lower than the mean value (44 kg) of the age-specific reference population (60-69 years) described by Steiber.[14]

Our study has some limitations. We could not include a follow up analysis after the initial 3-week hospitalised urooncological rehabilitation programme. Therefore, our results can only give an early picture of BIVA pattern and physical functional status in the rehabilitation process and survivorship pathway. Another limitation was the small sample size in some age and BMI related subgroups. Studies with larger sample sizes are necessary to confirm the current results. Moreover, because of a missing control group our study design does not allow to draw firm conclusions about the effectiveness of urooncological rehabilitation.

Conclusions

This study presents initial findings about a BIVA pattern in PCS and the occurrence of critical prognostic values of physical function at an early stage of cancer survivorship. The BIVA pattern differ significantly from population-based reference data and indicate an abnormal physiology. Combined with the prevalence of critically low HGS and PhA values our findings illustrate the necessity for intensive continuation of rehabilitation and survivorship care especially in these 'at risk' cases. Moreover, our data has shown that an inpatient 3-week rehabilitation programme improves muscular strength but without affecting the body cell mass. The routine assessment of BIVA, PhA and handgrip strength offer the opportunity to conduct a risk stratification for PCS and could help personalising and optimising treatment in rehabilitation and ongoing survivorship care.

Author Contributions

AS performed data management and analysis, manuscript writing and edition; MH performed data collection and data management; SG helped in data analysis; NG helped in manuscript editing; DHZ, PRW and HS provided editorial assistance and scientific oversight for the manuscript. All authors have read and approved the final manuscript.

Ethical Approval and Consent to Participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University of Technology (V-182-17-AS-Tumor-20012017). Written informed consent was obtained from all individual participants included in this study.

ORCID iD

Alexander Stäuber https://orcid.org/0000-0001-8744-236X

Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Supplemental Material

Supplemental material for this article is available online.

REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin*. 2011;61:69–90.
2. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136:E359–E386.
3. Brenner H, Arndt V. Long-term survival rates of patients with prostate cancer in the prostate-specific antigen screening era: population-based estimates for the year 2000 by period analysis. *J Clin Oncol*. 2005;23:441–447.
4. Galvão DA, Taaffe DR, Spry N, Joseph D, Turner D, Newton RU. Reduced muscle strength and functional performance in men with prostate cancer undergoing androgen suppression: a comprehensive cross-sectional investigation. *Prostate Cancer Prostatic Dis*. 2009;12:198–203.
5. Andriole GL. The impact of prostate cancer and hormonal therapy on bone. *Rev Urol*. 2009;11:185–189.
6. Cellina M, Martinenghi C, Gibelli D, et al. Secondary lymphedema following radical prostatectomy: noncontrast magnetic resonance lymphangiography assessment and vascularized lymph node transfer. *Ann Plast Surg*. 2020;85: e12–e18.
7. Sebesta EM, Anderson CB. The surgical management of prostate cancer. *Semin Oncol*. 2017;44:347–357.
8. Brown JC, Harhay MO, Harhay MN. Physical function as a prognostic biomarker among cancer survivors. *Br J Cancer*. 2015;112:194–198.

9. Kilgour RD, Vigano A, Trutschnigg B, Lucar E, Borod M, Morais JA. Handgrip strength predicts survival and is associated with markers of clinical and functional outcomes in advanced cancer patients. *Support Care Cancer*. 2013;21: 3261–3270.

10. Norman K, Stobäus N, Zocher D, et al. Cutoff percentiles of bioelectrical phase angle predict functionality, quality of life, and mortality in patients with cancer. *Am J Clin Nutr*. 2010;92:612–619.

11. Rick O, Dauelsberg T, Kalusche-Bontemps E-M. Oncological rehabilitation. *Oncol Res Treat*. 2017;40:772–777.

12. Bohannon RW. Muscle strength: clinical and prognostic value of hand-grip dynamometry. *Curr Opin Clin Nutr Metab Care*. 2015;18:465–470.

13. Rijk JM, Roos PR, Deckx L, van den Akker M, Buntinx F. Prognostic value of handgrip strength in people aged 60 years and older: a systematic review and meta-analysis. *Geriatr Gerontol Int*. 2016;16:5–20.

14. Steiber N. Strong or weak handgrip? Normative reference values for the German population across the life course stratified by sex, age, and body height. *PLoS One*. 2016;11:e0163917.

15. Celis-Morales CA, Welsh P, Lyall DM, et al. Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. *BMJ*. 2018;361:k1651.

16. Norman K, Stobäus N, Pirlich M, Bosy-Westphal A. Bioelectrical phase angle and impedance vector analysis-clinical relevance and applicability of impedance parameters. *Clin Nutr*. 2012;31:854–861.

17. Baumgartner RN, Chumlea WC, Roche AF. Bioelectric impedance phase angle and body composition. *Am J Clin Nutr*. 1988;48:16–23.

18. Piccoli A, Rossi B, Pillon L, Bucciante G. A new method for monitoring body fluid variation by bioimpedance analysis: the RXc graph. *Kidney Int*. 1994;46: 534–539.

19. Bosy-Westphal A, Danielzik S, Dörhöfer R-P, Later W, Wiese S, Müller MJ. Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. *J Parenter Enteral Nutr*. 2006;30:309–316.

20. Marini E, Buffa R, Saragat B, et al. The potential of classic and specific bioelectrical impedance vector analysis for the assessment of sarcopenia and sarcopenic obesity. *Clin Interv Aging*. 2012;7:585–591.

21. Castillo-Martínez L, Colín-Ramírez E, Orea-Tejeda A, et al. Cachexia assessed by bioimpedance vector analysis as a prognostic indicator in chronic stable heart failure patients. *Nutrition*. 2012;28:886–891.

22. Buffa R, Saragat B, Succa V, et al. Elderly subjects with type 2 diabetes show altered tissue electrical properties. *Nutrition*. 2013;29:132–137.

23. Piccoli A; Italian CAPD-BIA Study Group. Bioelectric impedance vector distribution in peritoneal dialysis patients with different hydration status. *Kidney Int*. 2004;65:1050–1063.

24. Piccoli A, Brunani A, Savia G, et al. Discriminating between body fat and fluid changes in the obese adult using bioimpedance vector analysis. *Int J Obes Relat Metab Disord*. 1998;22:97–104.

25. Walter-Kroker A, Kroker A, Mattiucci-Guehlke M, Glaab T. A practical guide to bioelectrical impedance analysis using the example of chronic obstructive pulmonary disease. *Nutr J*. 2011;10:35.

26. Haas V, Riedl A, Hofmann T, et al. Bioimpedance and bioimpedance vector analysis in patients with anorexia nervosa. *Eur Eat Disord Rev*. 2012;20: 400–405.

27. Nwosu AC, Mayland CR, Mason S, et al. Bioelectrical impedance vector analysis (BIVA) as a method to compare body composition differences according to cancer stage and type. *Clin Nutr ESPEN*. 2019;30:59–66.

28. Toso S, Piccoli A, Gusella M, et al. Bioimpedance vector pattern in cancer patients without disease versus locally advanced or disseminated disease. *Nutrition*. 2003;19:510–514.

29. Toso S, Piccoli A, Gusella M, et al. Altered tissue electric properties in lung cancer patients as detected by bioelectric impedance vector analysis. *Nutrition*. 2000;16:120–124.

30. Malecka-Massalska T, Smolen A, Zubrzycki J, Lupa-Zatwarnicka K, Morshed K. Bioimpedance vector pattern in head and neck squamous cell carcinoma. *J Physiol Pharmacol*. 2012;63:101–104.

31. Małecka-Massalska T, Chara K, Smolen A, Kurylcio A, Polkowski W, Lupa-Zatwarnicka K. Bioimpedance vector pattern in women with breast cancer detected by bioelectric impedance vector analysis. Preliminary observations. *Ann Agric Environ Med*. 2012;19:697–700.

32. Piccoli A, Pillon L, Dumler F. Impedance vector distribution by sex, race, body mass index, and age in the United States: standard reference intervals as bivariate Z scores. *Nutrition*. 2002;18:153–167.

33. Naranjo-Hernández D, Reina-Tosina J, Min M. Fundamentals, recent advances, and future challenges in bioimpedance devices for healthcare applications. *J Sens*. 2019;2019:1–42.

34. Schüle K. Thirty years of physical activity in oncology in Germany—from the birth of the first rehabilitative cancer sports group until today. *Eur Rev Aging Phys Activity*. 2013;10:61–64.

35. Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age Ageing*. 2011;40:423–429.

36. Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Front Psychol*. 2013;4:863.

37. Keeley V. Drugs that may exacerbate and those used to treat lymphoedema. *J Lymphoedema*. 2008;3:57–65.

38. Souza MF, Tomeleri CM, Ribeiro AS, et al. Effect of resistance training on phase angle in older women: a randomized controlled trial. *Scand J Med Sci Sports*. 2017;27:1308–1316.

39. Ribeiro AS, Nascimento MA, Schoenfeld BJ, et al. Effects of single set resistance training with different frequencies on a cellular health indicator in older women. *J Aging Phys Act*. 2018;26:537–543.

40. Chen Z, Zhang Y, Lu C, Zeng H, Schumann M, Cheng S. Supervised physical training enhances muscle strength but not muscle mass in prostate cancer patients undergoing Androgen deprivation therapy: a systematic review and meta-analysis. *Front Physiol*. 2019;10:843.

41. Barbosa-Silva MC, Barros AJ, Wang J, Heymsfield SB, Pierson RN. Bioelectrical impedance analysis: population reference values for phase angle by age and sex. *Am J Clin Nutr*. 2005;82:49–52.