Evaluation of preoperative bioimpedance spectroscopy quantification of body composition on predicting postoperative outcomes following robotic assisted radical prostatectomy (RARP)

Gina M. Badalato, MD,[1] Matthew S. Wosnitzer, MD,[1] Matthew D. Truesdale, MD,[1] Marco Sandri, MD,[2] Woo Jin Ko, MD,[1] Jaime Landman, MD,[1] Ketan K. Badani, MD[1]

[1]Department of Urology, Columbia University Medical Center, New York, New York, USA

[2]Libera Università di Lingue e Comunicazione, Milan, Italy

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Introduction: *Bioimpedance spectroscopy (BIS) is a novel, precise quantification of body composition (BC) using low electrical currents through tissue. Accurate BC quantification may better predict postoperative outcomes. We compared BIS-BC and body mass index (BMI) for correlation with post-surgical outcomes in robotic assisted radical prostatectomy (RARP) patients.*

Materials and methods: *Preoperative BIS-BC and BMI analyses were conducted on men with biopsy-proven prostate cancer undergoing RARP. Height, weight, percentage and fat mass (PFM, FM), percentage and fat-free mass (PFFM, FFM), percentage and total body water (PTBW, TBW), and percentage and intracellular/extracellular water (PICW, PECW, ICW, ECW) were obtained using the ImpediMed SFB7 Device (San Diego, CA, USA). Preoperative PSA, biopsy and pathologic Gleason scores, prostate volume, percentage tumor volume, margin status, operative time, estimated blood loss (EBL) and pathologic stage were recorded. Spearman's rank correlation was estimated to evaluate the association between BIS-BC results, BMI, and post-surgical outcomes.*

Results: *Between April 2009 and August 2010, 63 men had been enrolled in this ongoing study. Fourteen were of normal weight (18.5 kg/m^2-24.9 kg/m^2), 33 were overweight (25 kg/m^2-29.9 kg/m^2) and 16 were obese (BMI ≥ 30 kg/m^2). Mean age was 60.7 years, mean preoperative PSA was 7.4 ng/mL, and median Gleason was 7. BMI correlated with FFM ($p = 0.002$), FM ($p = 0.01$), and PTBW ($p = 0.02$). FM correlated with preoperative PSA ($p = 0.01$). PFFM ($p = 0.03$), PFM ($p = 0.03$) and PTBW ($p = 0.04$) correlated with % tumor volume. ICW ($p = 0.01$) and TBW ($p = 0.009$) correlated with EBL. BMI ($p = 0.04$), PECW ($p = 0.04$), FM ($p = 0.05$), and PICW ($p = 0.03$) correlated with pathologic tumor stage.*

Conclusions: *BMI correlates with BIS-BC FFM, FM and PTBW. PFFM, PFM and PTBW correlated with % tumor volume. ICW and TBW correlated with EBL. BMI, PECW, FM, and PICW correlated with pathologic tumor stage. BIS-BC metrics may be helpful in predicting post-RARP outcomes. Further study is required to validate these predictions.*

Key Words: malignant disease, robotics, prostate, laparoscopy

Introduction

Clinical studies have indicated a correlation exists between obesity metrics and oncologic outcomes. To date, however, these investigations have relied upon a body mass index (BMI) measurement, which remains a crude metric based on patient height and weight alone.[1,2]

The inception of bioimpedance spectroscopy (BIS) introduced a novel, precise tool that might be used in the quantification of body composition (BC) using low electrical currents through tissue. In fact, this instrument can exactly quantify BC by passing low electrical currents through tissue mass and extrapolating data from bioelectrical impedance analysis (BIA) of current flow resistance.[3,4]

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Address correspondence to Dr. Gina M. Badalato, Department of Urology, Columbia University Medical Center, 161 Fort Washington Avenue, Herbert Irving Pavilion, New York, NY 10032

Accordingly, this study sought to determine if accurate body fat composition determination prior to robot-assisted radical prostatectomy (RARP) might enhance prognostic information. Specifically, an evaluation of the correlation between BIS BC metrics with BMI was first performed to determine the relative concordance of these anthropometric measurements in pre-operative RARP patients. BIS-BC and BMI metrics were then evaluated for correlation with post-surgical outcomes in patients following RARP.

Materials and methods

Preoperative BIS-BC and BMI analyses were conducted on men with biopsy-proven prostate cancer undergoing RARP. Study participation was voluntary and all patients received informed consent prior to procedure initiation; furthermore, this investigation was carried out under the purview of an IRB-approved protocol. BIS-BC and BMI values were obtained immediately before surgery using the ImpediMed SFB7 Device (San Diego, CA), Figure 1. To use this apparatus, the patient was first positioned supine on a non-metallic surface. Clean sites on the dorsum of the hand and ipsilateral foot were then identified for electrode placement and lead attachment. Height, weight, percentage and fat mass (PFM, FM), percentage and fat-free mass (PFFM, FFM), percentage and total body water (PTBW, TBW), and percentage and intracellular/extracellular water (PICW, PECW, ICW, ECW) were then calculated using this device.

Clinical and pathologic variables of preoperative PSA, biopsy and pathologic Gleason scores, prostate volume, percentage tumor volume, extracapsular extension, lymph node status, margin status, operative time, estimated blood loss (EBL) and pathologic stage were recorded. Spearman's rank correlation was

Figure 1. ImpediMed SFB7 Device and electrode placement on dry skin of dorsum of hand and foot. Courtesy of ImpediMed, Inc.

TABLE 1. **Baseline clinical and operative characteristics of the patient cohort**

Variable	Value
Mean age	60.7 ± 6.6 years
Mean height	69.7 ± 4.3 in
Mean weight	193.4 ± 28.2 lbs
Mean BMI	28.4 ± 4.2 kg/m^2
Mean pre-PSA	7.4 ± 8.5 ng/mL
Median Bx Gleason	7 (range: 6-9)
Mean prostate weight	53.2 ± 19.1 g
Mean tumor size	13.8 ± 16.3 cc
Mean OR time	174.7 ± 42.6 min
Mean EBL	157.3 ± 105.9 mL

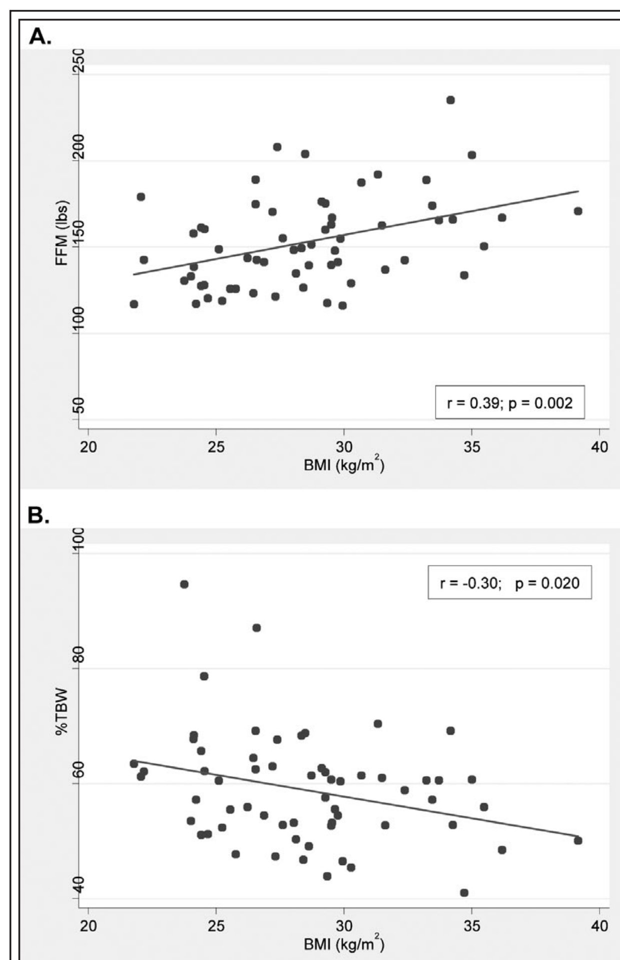

Figure 2. Scatter plots of BMI and FFM (A) and BMI and percent PTBW (B) both demonstrated statistically significant Spearman's rank correlations.

TABLE 2. **Association of BMI and BIS BC metrics and postoperative outcomes. The top number is the estimated Spearman's rank correlation. The bottom number is the p value for the associated hypothesis test of independence.**

	Prostate size	Pathologic Gleason sum	Pathologic tumor stage	% tumor volume	OR time	EBL
BMI	-0.03 p = 0.8	0.001 p = 0.9	0.3 p = 0.04	0.01 p = 0.9	0.1 p = 0.4	0.06 p = 0.7
FFM	0.14 p = 0.3	0.01 p = 0.7	0.09 p = 0.5	-0.08 p = 0.5	0.15 p = 0.3	0.2 p = 0.1
PFFM	0.14 p = 0.3	0.05 p = 0.2	-0.2 p = 0.2	-0.3 p = 0.03	0.05 p = 0.7	0.1 p = 0.3
FM	-0.05 p = 0.7	0.06 p = 0.1	0.3 p = 0.05	0.2 p = 0.07	-0.02 p = 0.9	-0.1 p = 0.4
PFM	-0.13 p = 0.3	0.05 p = 0.2	0.2 p = 0.2	0.3 p = 0.03	-0.05 p = 0.7	-0.2 -p = 0.3
TBW	-0.12 p = 0.3	0.04 p = 0.3	0.02 p = 0.9	0.03 p = 0.8	-0.07 p = 0.6	0.2 p= 0.009
PTBW	0.07 p = 0.6	0.004 p = 0.9	-0.2 p = 0.1	-0.26 p = 0.04	0.03 p = 0.8	0.1 p = 0.4
ICW	-0.15 p = 0.2	0.04 p = 0.3	-0.04 p = 0.8	0.000 p = 0.9	-0.05 p = 0.7	0.3 p = 0.01
PICW	-0.01 p = 0.9	0.02 p = 0.5	-0.3 p = 0.03	-0.23 p = 0.08	0.04 p = 0.8	0.2 p = 0.2
ECW	-0.12 p = 0.3	0.04 p = 0.3	0.1 p = 0.4	0.01 p = 0.9	-0.04 p = 0.8	0.2 p = 0.08
PECW	0.05 p = 0.7	0.03 p = 0.4	0.3 p = 0.04	0.2 p = 0.1	0.01 p = 0.9	-0.1 p = 0.4

estimated to evaluate the association between BIS-BC results, BMI, and post-surgical outcomes. Two-sided p values < 0.05 were considered statistically significant. All analyses were conducted using Stata software (StataCorp. 2009. Stata Statistical Software: Release 11; StataCorp LP, College Station, TX, USA).

Results

Between April 2009 and August 2010, 63 men had been enrolled in this ongoing study. Of all the subjects, 14 were of normal weight (18.5 kg/m^2-24.9 kg/m^2), 33 were overweight (25 kg/m^2-29.9 kg/m^2) and 16 were obese (BMI ≥ 30 kg/m^2). The mean age was 60.7 +/- 6.6 years, the mean preoperative PSA was 7.4 +/- 8.5 ng/mL, and the median Gleason at biopsy was 7 (range: 6-9), Table 1. In terms of operative variables for the aggregate, the mean total operative time for RARP was 174.7 +/- 42.6 minutes and the mean EBL was 157.3 +/- 105.9 cc.

The Spearman's rank correlation results calculated for each anthropometric measurement and the associated postoperative outcomes are displayed in Table 2. In terms of comparison within different body composition metrics, BMI correlated with FFM (r = 0.4, p = 0.002), FM (r = 0.3, p = 0.01), and PTBW (r = -0.3, p = 0.02). The estimated linear relationship amongst the aforementioned variables is graphically represented in Figure 2.

When evaluating operative and oncologic outcomes, however, the BIS-BC metrics presented novel relationships that were not approximated by BMI alone, Table 2. Accordingly, FM correlated with preoperative PSA (r = 0.3, p = 0.01). PFFM (r = -0.3, p = 0.03), PFM (r = 0.3, p = 0.03) and PTBW (r = -0.26, p = 0.04) was associated with percentage tumor volume.

Also, the operative parameter of EBL was correlated with ICW ($r = 0.3$, $p = 0.01$) and TBW ($r = 0.2$, $p = 0.009$). While BMI maintained an independent association with pathological tumor stage ($r = 0.3$, $p = 0.04$), several other BIS-BC indices were also linked to this variable, namely PECW ($r = 0.3$, $p = 0.04$), FM ($r = 0.3$, $p = 0.05$), and PICW ($r = -0.3$, $p = 0.03$). Lastly, no association between lymph node status, margin status, or extracapsular extension was noted with BMI or other BIS-BC measurements.

Discussion

Multiple studies have demonstrated an association between obesity and an increased risk of higher grade prostate cancer as well as a higher PSA recurrence following radical prostatectomy.[1,5,6] Nevertheless, many of these antecedent studies have relied upon BMI alone, a simple measurement of body composition, to establish the precedent of this risk relationship. Because of the reliance on imprecise measurements of body composition, the current accepted risk relationship between prostate cancer and obesity may be inaccurate and/or imperfect. In this vein, this study sought to use BIS-BC metrics, a novel tool for the measurement of body mass composition, to determine if these values significantly correlated with clinical, oncologic, and perioperative variables in patients undergoing RARP. By using this innovative tool, this investigation determined that BIS-BC measurements did correlate with many postoperative outcomes, many of which would not have been recognized by measurement of BMI alone, and these indices may thus be helpful in preoperative patient risk stratification.

The prevalence of obesity has been rising over the last several decades, with 30% of men in the United States qualifying as obese.[7] While the public health impact of this trend is irrefutable, the modulatory role of body habitus on prostate cancer remains somewhat controversial. Although several series have demonstrated obesity may be linked to a lower incidence of disease,[8-10] it is clear that adiposity is associated with a greater risk of prostate cancer-related death.[9,11] Large meta-analyses have compounded these findings by establishing the correlation between a higher BMI and an increased risk of cancer recurrence after radical prostatectomy.[1,5,6]

Bioimpedance methods rely upon an electrical model of tissues and resistances; importantly, this analysis offers a new avenue whereby body fluid volumes might be accurately measured non-invasively based on empiric equations of the wrist-ankle resistance.[12-14] Within the field of nephrology, bioimpedance measurements have been utilized as a reliable method of determining the hydration state of hemodialysis patients because of the dynamic fluid shifts that occur with treatment.[15,16] The European Society for Parenteral and Enteral Nutrition (ESPEN) has further recommended BIS-BC metrics as important data points which may contribute to improvements in clinical practice.[3,4] Accordingly, as a marker of nutritional status, BIS has been used to improve the survival prognostication for patients receiving palliative care for cancer. In fact, results of a recent study within this palliative patient population indicated that an accumulation of total body fluid was a poor predictor of survival, and, as a marker of this endpoint, BIS may be a useful, noninvasive assessment tool for early nutritional deterioration.[17]

Because of the growing body of evidence that BIS provides useful information on body composition as well as evidence that this tool has important applications within other fields of medicine, it is appropriate that these metrics be applied within the pre-surgical prostate cancer patient population, a group of patients where obesity has had a demonstrable role on cancer-related outcomes. This study sets the precedent for such a novel application, and establishes the link between several clinical outcomes and BIS metrics.

As stated, this investigation not only validated the strong correlation between BMI and other BIS-BC metrics, but it also established significant relationships between these indices and other perioperative measures. First, BMI trended with FM and other measures of percent body water distribution in the determination of patient pathologic stage. This finding is in concordance with prior investigations that have determined obesity, as measured by BMI, is a risk factor for higher grade tumors.[1] The biological and molecular underpinnings for this phenomenon are not discrete. Several different mechanisms including hyperinsulinemia with consequent lower sex hormone-binding globulin and an increase in bioavailable testosterone have been postulated to be involved in the cascade contributing to higher in vitro mitogenic activity.[18-22] These factors perhaps in combination with dietetic factors, such as a food high in fatty acid and associated linoleic acid content, may contribute to this risk.[23-25] The molecular and physiologic mechanisms underlying adiposity may explain why the percentage tumor volume correlated so significantly with relative measurements of fat mass but not BMI per se; in fact, percentage tumor volume was associated with PFM and PFFM in addition to PTBW. Likewise, a direct association was again noted with fat mass, this time as an absolute variable, when it was determined to be significantly related to the preoperative

PSA value. Although these associations are relatively clear, the rationale for the final correlation noted between EBL and intra- and extracellular water content is less obvious. The higher blood loss cannot be purely interpreted as a proxy marker for a procedure requiring greater technical prowess, because the total operative time was not associated with these BIS metrics. One possible explanation for these findings is that intra- and extracellular water content is commensurate with total circulating blood volume and possibly hypervascularity, thus creating a greater bleeding potential.

Interestingly, margin status and extracapsular extension were not significantly associated with anthropometric measurements. The risk of positive surgical margins has remained controversial among obese patients undergoing prostatectomy, although much of this literature is based on open prostatectomy techniques.[1,26-28] In one of the seminal articles on the impact of obesity on biochemical control after open radical prostatectomy, Freedland et al noted a higher incidence of positive surgical margins, in the absence of extracapsular extension, among the obese subset.[1] In the absence of other adverse pathologic features, the authors determined the technical difficulty during the surgical dissection of the prostate among obese men might have been one of the factors contributing to this outcome. Taken together with these determinations, perhaps the findings showing body habitus to be an insignificant predictor of margin status could indicate that operative approaches, particularly within the robotic system, are improving to afford better oncologic outcomes among obese patients.

In terms of future directions, this study is limited by the relatively small sample size and the fact that associations between BIS-BC determinations with prostate cancer require validation in larger cohorts. Furthermore, as the impact of anthropometric factors on the pathogenesis of prostate cancer continues to be characterized, consideration should be given to inclusion of bioimpedance measurements, and not BMI alone, within these investigations.

In conclusion, BIS indices are a more precise characterization of body composition than BMI alone, and several significant associations between these metrics and clinical and operative outcomes were noted among patients undergoing RARP. Specifically, BMI, PECW, FM, and PICW correlated with pathologic tumor stage. PFFM, PFM and PTBW correlated with percentage tumor volume. Finally, ICW and TBW correlated with EBL. These findings substantiate that BIS-BC metrics may be useful in predicting post-RARP outcomes; accordingly, further study is required to quantify the strength of these associations. □

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