Body composition and mortality in men receiving prostate radiotherapy: a pooled analysis of NRG/RTOG 9406 and NRG/RTOG 0126

Short title: Body composition in prostate cancer

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Conflict of Interest

Dr's Bahary, Chen, Den, Dess, Doncals, Hoyle, Lau, Lenzie, Macrom, McDonald, Mendez, Michalski, Parliament, Pugh, Roach, Valicenti, and Lyudmila DeMora, MS have no conflicts of interest to declare. Dr. Feng reports consulting fees from Janssen, Bayer, PFS Genomics (termed April 2021), Myovant Sciences, Roivant Sciences, Astellas, Foundation Medicine, Varian, Bristol Meyers Squibb, Exact Sciences, and Novartis, receipt of stock options from Serimmune from serving on their scientific advisory board in 2020, payment or honoraria from Bristol Meyers Squibb for two educational presentations. Dr. Feng reports his Co-Founder role at Artera, where he does not receive a salary, funding or consulting fees from the company - only shares. He reports a leadership position with NRG Oncology, where he serves as the Chair of the Genitourinary Cancer Committee. His role at NRG helps investigators design proposals for clinical trials, that are then evaluated by the NCI for funding. All funding decisions are made by the NCI – not by NRG or by Dr. Feng. Dr. Mishra reports support for attending meetings and/or travel from Varian Medical Systems. Dr. Sandler reports consulting fees for his role as a member of the clinical trial steering committee for Janssen; he is also a member of the Board of Directors for ASTRO. Dr. Souhami reports travel support from Varian Medical Systems and his participation on a Data Safety Monitoring Board or Advisory Board for AbbVie and Janssen. Dr. Williams reports consulting fees from Cardinal Health and Carevive and payment or honoraria for presentations from Cardinal Health. Dr. Yang reports grants or contract from Eli Lilly and Puma Biotechnologies to UAB, and his participation on a Data Safety Monitoring Board or Advisory Board for Astrazeneca, Bayer, and Clovis.

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Precis

This study strongly supports that body composition is related to mortality in men with localized PCa. The inclusion of psoas area in the RPA classification tree suggests that body composition provides additive information to age and comorbidity status for mortality prediction, particularly among older men.

ABSTRACT

Background: To validate the association between body composition and mortality in men treated with radiation for localized prostate cancer (PCa). Secondarily, to integrate body composition as a factor to classify patients by risk of all-cause mortality.

Materials and Methods: Participants of NRG/RTOG 9406 and NRG/RTOG 0126 with archived computed tomography were included. Muscle mass and muscle density were estimated by measuring the area and attenuation of the psoas muscles on a single slice at L4-L5. Bone density was estimated by measuring the attenuation of the vertebral body at mid-L5. Survival analyses, including Cox proportional hazards models, assessed the relationship between body composition and mortality. Recursive partitioning analysis (RPA) was utilized to create a classification tree to classify participants by risk of death.

Results: Data from 2,066 men was included in this study. In the final multivariable model, psoas area, comorbidity score, baseline prostate serum antigen, and age were significantly associated with survival. The RPA yielded a classification tree with 4 prognostic groups determined by age, comorbidity, and psoas area. Notably, the classification among older (≥70 years) men into prognostic groups was determined by psoas area.

Conclusions: This study strongly supports that body composition is related to mortality in men with localized PCa. The inclusion of psoas area in the RPA classification tree suggests that body composition provides additive information to age and comorbidity status for mortality prediction, particularly among older men. More research is needed to determine the clinical impact of body composition on prognostic models in men with PCa.

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Key Words: Prostate cancer, body composition, anthropometry, muscle mass, mortality, clinical trials

INTRODUCTION

Modern treatment for localized prostate cancer (PCa) is highly effective, and current 10-year PCa specific mortality rates are less than 10% even when high-risk features are present.[1-6] Overall survival among men with localized PCa is instead driven by competing causes of death, which has important ramifications for both patient care and clinical trial design.[7-10] Tools to predict the risk of mortality from competing risks have an important role for research and clinical care, but ongoing refinement of risk prediction models is needed to improve their accuracy.

Body composition is a biomarker of overall health that may provide additional prognostic information to improve current risk prediction models for mortality among men with PCa. Prior research investigating the relationship between body mass index (BMI) and mortality has been mixed, particularly when accounting for medical comorbidities.[11-13] More focused measurements of body composition such as fat mass, muscle mass, and bone density, can be used as an alternative to BMI and conventional anthropometry. While a variety of methods can be used to assess body composition, cross-sectional imaging is increasingly utilized due to the advantage of being able to assess adipose, muscle, and bone simultaneously using imaging that is already obtained as part of routine care. A prior study reported that body composition measurement using radiotherapy computed tomography (CT) simulation scans was feasible and provided additional information to improve non-PCa mortality risk prediction, but the study was limited to a single institution and has not been validated.[14] The primary purpose of the present study was to further investigate whether measurement of body composition provides additional information to improve mortality risk assessment for men with PCa who participated in NRG/RTOG clinical trials.

Body composition measurement using cross-sectional imaging also enables post-hoc measurements using archived clinical trial data to explore if body composition modulates the effects of treatment variables on outcomes. One area of ongoing debate is whether androgen deprivation (ADT) increases mortality risk for some men.[15-19] Since ADT is known to have significant detrimental effects on male body composition, we

also sought to explore whether men who have an unfavorable body composition phenotype experience worse survival outcomes when receiving ADT.[20,21]

METHODS AND MATERIALS

Inclusion criteria and regulatory approval: This study included all participants of NRG/RTOG 9406 and NRG/RTOG 0126 who had archived CT scans that extended cranially to include the L4-L5 interface and were without significant artifact. The full details of these 2 clinical trials have been previously published.[5,22] NRG/RTOG 9406 enrolled men who had T1-T3 PCa and were assigned to one of five radiation dose levels; neoadjuvant ADT for up to 6 months was allowed. NRG/RTOG 0126 enrolled men with intermediate risk PCa and were assigned to one of two radiation dose levels; no ADT was allowed. The present study was approved by the University of Alabama at Birmingham Institutional Review Board.

Body composition measurement: CT analysis was performed using MIM software (MIM Software Inc., Cleveland, OH, USA). Estimates of muscle mass, muscle density, bone density, and subcutaneous adipose density were calculated. The cross-sectional areas of all skeletal muscle at the L4-L5 interface, as well as the area of the paired psoas muscles, were used as surrogates for total body muscle mass. The cross-sectional area of skeletal muscle at the L4-L5 interface has previously been shown to have very high concordance with total body lean mass, and psoas area has also strongly been associated with survival outcomes in a number of populations.[23,24] Total skeletal muscle and the paired psoas muscles were separately segmented on a single slice , post-processed to include only those voxels with Hounsfield unit (HU) between -29 and 150 to exclude fatty infiltration, and area (cm^2) recorded (**Supplemental Figure 1**). The CT attenuation of the paired psoas muscles was calculated on the single slice at the L4-L5 interface as a marker of myosteatosis.[25]

The CT attenuation of the trabecular bone of the L5 vertebral body was used a surrogate for bone mineral density (BMD) and has previously been shown to have high concordance with BMD assessed by dual x-ray absorptiometry.[26] The trabecular bone of the vertebral body was segmented at the slice bisecting mid-L5, with care taken to avoid any abnormalities such as bone islands or vascular channels, and the mean HU of the resulting region-of-interest was recorded.

Subcutaneous adipose tissue density is a measure of fat quality that has previously been found to be associated with all-cause mortality in 2 large population registry studies.[27] In our study we measured subcutaneous adipose tissue density on a single slice at the L4-L5 interface. The adipose tissue outside of the abdominal cavity was segmented and post-processed to include only those voxels with HU between -195 and -45HU, and the mean HU of the resulting region-of-interest was recorded.

Endpoints and statistical methods: Body composition measurements were analyzed as continuous and categorical variables. Unadjusted psoas and skeletal muscle areas were utilized for analysis since patient height was not available. Psoas area was categorized into tertiles (<25.2cm^2, 25.2 to <29.9cm^2, and ≥29.9 cm^2) as was psoas density (<35.6HU, 35.6 to <46.9HU, ≥46.9HU). L5 vertebral radiodensity was categorized into 3 intervals (<105HU, 105 to <150HU, ≥150HU) which have been previously utilized.[26,28] Adipose radiodensity was categorized into 4 intervals (<-104HU, -104 to <-99.5HU, -99.5 to <-95HU, ≥-95HU).[29] Comorbidity information was abstracted from trial registration forms and comorbidity score was obtained by assigning 1 point for the presence of each of 14 problems listed (**Supplemental Table 1 and 2)**.

Between group differences were tested using the Kruskal-Wallis test for continuous variables and Chi-square test for categorical variables. Overall survival (OS) was measured from randomization to the date of death or censored at the last known follow-up for alive patients. OS was estimated using the Kaplan-Meier method and between group differences were tested using the log-rank test. PCa specific mortality (PCSM) was measured from the date of randomization to the date of death due to PCa or study treatment

(determined by the institution). Patients who died without an event for PCSM were treated as a competing risk and alive patients were censored. Time to PCSM was estimated using cumulative incidence with between group differences tested using Gray's test. Freedom from biochemical failure (FFBF) was assessed from randomization to the date of biochemical failure using the RTOG-Phoenix definition.[30] Cox proportional hazards models for OS, and cause-specific Cox proportional hazards models for time to PCSM and biochemical failure, were used to obtain unadjusted and adjusted hazard ratios (HRs) and 95% confidence intervals (CIs). Correlations between the body composition variables, to avoid collinearity in the models, was assessed using Pearson correlation coefficients and variance inflation factor. Adjusted models also assessed the impact of variables of interest while adjusting for other possible confounders, such as age, comorbidity status, and induction ADT. A final multivariable model included body composition variables that were significant in adjusted models, after assessing for collinearity. Recursive partitioning analysis (RPA), using the R package rpart, was used to create a classification tree based on risk of death.[31] All variables from the final multivariable model were included in the RPA to build the classification tree. The classification tree was built using NRG/RTOG 0126 data and validated, using Cox proportional hazards models, in NRG/RTOG 9406 data.

RESULTS

Patient characteristics: Of the 2,616 men enrolled on the NRG/RTOG 9406 and NRG/RTOG 0126 clinical trials, 2,066 (79.0%) had archived CT scans available that were suitable for body composition assessment and were included in this study. Demographic and disease characteristics are presented in **Table 1**. The summary statistics of the body composition analysis is presented as **Table 2**. Patients on NRG/RTOG 9406, as compared to the NRG/RTOG 0126 70.2Gy arm and the NRG/RTOG 0126 79.2 Gy arm had lower skeletal muscle area and higher adipose tissue density. NRG/RTOG 9406, as compared to the NRG/RTOG 0126

70.2Gy arm and the NRG/RTOG 0126 79.2 Gy arm, had fewer patients with vertebral body density <105 HU. The correlation matrix of body composition variables is presented as **Supplemental Table 3**.

Survival Outcomes: A total of 539 deaths were recorded in the NRG/RTOG 0126 cohort and 307 deaths were recorded in the NRG/RTOG 9406 cohort. Cause of death was related to PCa for 68 (8%) men, treatment complications for 1 (0.1%) man, non-PCa causes for 510 (60.3%) men, and unknown causes for 267 (31.6%) men (**Supplemental Table 4**).

Higher psoas area was significantly associated with improved survival in both the unadjusted and adjusted models (HR=0.770 (95%CI: 0.656-0.904) for 25.2-29.9cm^2 vs. <25.2cm^2, p=0.001 and HR=0.698 (95%CI: 0.587-0.829) for ≥29.9cm^2 vs. <25.2cm^2, p<0.001 after adjusting for patient characteristics). The highest category of vertebral body density was associated with improved survival when compared to the lowest category (HR=0.788 (95%CI: 0.653-0.951) for ≥150HU vs. <105HU, p=0.013). Categorical psoas density, skeletal muscle area, and subcutaneous adipose density were not significantly associated for survival in the adjusted models. **Figure 1** presents the Kaplan-Meier survival estimates for the study cohort stratified by psoas area, vertebral body density, and adipose density.

The multivariable model of OS is shown in **Table 3**. Age (continuous, HR=1.055 (95%CI: 1.043-1.067), p<0.001), comorbidity score (HR=1.54 (95% CI: 1.337-1.773) for 1-2 vs. 0, p<0.001 and HR=2.573 (95% CI: 1.876-3.529) for 3-5 vs. 0, p<0.001), psoas area (HR=0.787 (95%CI: 0.669-0.926) for 25.2-<29.9 cm^2 vs. <25.2 cm^2, p=0.004 and HR=0.714 (95%CI: 0.599-0.852) for ≥29.9 cm^2 vs. <25.2 cm^2, p<0.001), and baseline PSA (continuous, HR=1.015 (95%CI: 1.004-1.026), p=0.0067) were each associated with overall mortality. The results of the RPA (**Figure 2**) classified the NRG/RTOG 0126 cohort into 4 prognostic subgroups based on risk of death. Notably, the classification into groups III and IV among older (≥70 years) men was determined by psoas area. The Kaplan-Meier estimates of OS stratified by RPA classification group in the NRG/RTOG 0126 cohort and the validation NRG/RTOG 9406 cohort were significant (p<0.001 for each cohort) are shown in **Figure 3**. The results of multivariable models for OS, PCSM, and FFBF with

continuous body composition variables are shown in **Supplemental Table 5**. Adipose density (continuous, HR=1.006 (95%CI: 1.000-1.011), p=0.035), vertebral body density (continuous, HR=0.998 (95%CI: 0.996-0.999), p<0.001), and psoas area (continuous, HR=0.979 (95%CI: 0.967-0.991), p<0.001) were each associated with OS when considered as a continuous variable. Adipose density (continuous, HR=1.027 (95%CI: 1.008-1.048), p=0.007) was associated with PCSM and no body composition variable was associated with FFBF.

Exploratory analysis of ADT and mortality: The Kaplan-Meier estimates of OS for patients receiving ADT versus no ADT, stratified by RPA classification, is shown in **Supplemental Figure 2**. No significant association between ADT use and mortality was observed within any of the RPA subgroups. No interaction between ADT and psoas area or vertebral body density was observed in a Cox proportional hazards model for OS (**Supplemental Table 6**).

DISCUSSION

We performed this study with the goal of expanding our understanding of how body composition and mortality are related in men with PCa. Studies that have investigated the relationship between anthropometry and mortality risk for men with localized PCa have been mixed. An association between BMI and mortality was not observed in a Cleveland Clinic cohort study of men receiving external beam RT, nor in a separate cohort study of men who were treated with brachytherapy.[11,12] More detailed clinical anthropometry was performed as part of a prospective cohort study of nearly 1,000 men in Alberta, Canada and no association was observed with either BMI, waist circumference, or waist-hip ratio and all-cause mortality.[32] In contrast, in the Cancer Prostate in Sweden study, BMI≥27.5 kg/m^2 was significantly associated with worse survival in a model incorporated age but not comorbidity status.[33] Nguyen et al. also observed higher rates of all-cause mortality among overweight and obese men with biochemically recurrent PCa, particularly among those with 0-1 documented comorbidities.[13]

The body composition descriptive characteristics of the present study cohort should be interpreted with the understanding that NRG/RTOG 9406 and NRG/RTOG 0126 enrolled men who were generally healthy, as opposed to other oncology populations where cachexia, myopenia, and sarcopenia are more common. The mean L5 radiodensity and psoas radiodensity were higher among the cohort of men from NRG/RTOG 9406, which is consistent with the fewer men with comorbidities in that trial as compared to NRG/RTOG 0126. Psoas area and mid-L5 vertebral body radiodensity were both significantly associated with overall survival when analyzed individually and in models that adjusted for age and comorbidity status. Psoas radiodensity and subcutaneous adipose radiodensity were additional candidate variables that were investigated as measures of myosteatosis and fat quality, respectively, but were not associated with mortality when considered as categorical variables.

Psoas area remained significantly associated with mortality in a multivariable model containing other body composition variables as well as age and comorbidities. L5 density and adipose density were significantly associated with mortality only when considered as continuous variables and not using the predefined categories. When available, predefined categories for body composition variables were used to enhance the validity of the study, but this approach has a risk of masking associations and further work is needed to understand the relationship between bone density, adiposity, and mortality among men with PCa. Additional models of PCSM and FFBF showed the expected impact of baseline PSA and Gleason score but no clear association with body composition, consistent with the hypothesis that the association between body composition and OS is driven by non-PCa mortality. The ability of body composition assessment to enhance patient prognostication was highlighted by the RPA model where psoas area was selected to discriminate the risk of mortality among men ≥70 years. The selection of psoas area as a decision point to stratify older patients is consistent with prior studies suggesting that muscle mass is an important factor associated with frailty and overall health among older adults with and without cancer.[34-36]

The ability to classify men with PCa by risk of mortality has important implications for patient care and research. One ongoing debate is whether some men with PCa experience increased mortality when receiving ADT. Men enrolled in a Harvard randomized trial of ADT who had moderate or severe comorbidities experienced worse OS if they received ADT.[15] ADT has also been associated with worse survival among men with cardiac comorbidity in a large multi-practice community cohort study,[16] and among African American men with intermediate risk disease treated at one center.[19] But these findings have been inconsistent, and other studies including the TROG 96.01 clinical trial and a population-based study of men receiving brachytherapy have not observed worse outcomes for men receiving ADT.[17,19] We investigated this topic by comparing survival among participants of NRG/RTOG 9406 who received ADT versus those who did not, stratified by the RPA classification of baseline risk of mortality. We hypothesized that stratification by RPA groups, which include muscle mass and comorbidities, may identify patients whose survival is negatively impacted by ADT. However, use of ADT was not associated with survival within any of the RPA subgroups and this remains an important topic for future research.

To our knowledge, this is the largest study of body composition among men with PCa and the first study that has simultaneously considered estimates of muscle mass, muscle quality, fat quality, and bone density. The observed relationship between psoas area and survival persisted after controlling for age and comorbidities, and the selection of psoas area by the RPA algorithm to classify patients supports that the additional prognostic information gained by assessing body composition is meaningful. Improving mortality risk prediction is not only clinically important but can aid in future research studies since stratifying by competing risks may improve clinical trial design and efficiency.[10] The use of the RPA classification to further investigate the relationship between ADT and mortality, while negative, provides important proof-of-principle that analysis of archived CT scans can leverage clinical trial data outcomes data to investigate new hypotheses.

A further strength of this study is the quality of the clinical trial data. Pre-treatment details were captured in a standardized fashion and patient outcomes were assessed prospectively. The use of data from two separate clinical trials also allowed for a natural division of training and validation cohorts which is less susceptible to bias. One limitation is that information about patient comorbidities was limited to what was available on the trial registration forms. Our approach of summing the number of comorbidities may be viewed as unconventional but is similar to how the Charlson Comorbidity Index score is derived.[37] Analyses of cause specific mortality were limited by the fact that cause of death was unknown for nearly one-third of decedents. Regarding the measurement of body composition, patient height that was not collected for these studies, thus skeletal muscle area and psoas areas were used for analysis rather than normalizing to skeletal muscle index or psoas index and weight was used instead of BMI. However, the results of the analysis with psoas area in this study were strongly consistent with prior studies that utilized psoas index, supporting that the unavailability of height information is unlikely to have altered the results. Due to the nature of CT protocols for PCa simulation scans, this study performed analysis at the level of L4-L5. While cross-sectional body composition analysis is more commonly performed at L3, measurements at L4-L5 are also validated and perform similarly to measurements at L3.[23]

In summary, this study demonstrated that baseline body composition, namely psoas cross-sectional area as a surrogate for muscle mass, is associated with mortality in men with PCa. The relationship between body composition and mortality may be particularly meaningful among older men. This study also confirmed the feasibility of using archived clinical trial data to investigate new hypotheses related to body composition. No subgroup was identified within this cohort where ADT increased mortality, but this remains an important area of ongoing research. Though more work is needed to clarify the clinical impact of body composition in men with PCa, recognizing the association between body composition and mortality may assist with patient selection and provide a target for lifestyle interventions to improve outcomes.

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FIGURE LEGEND TEXT

Figure 1. Kaplan-Meier survival estimates for the study cohort stratified by (a) psoas area, (b) vertebral body density, and (c) adipose density.

Figure 2. Recursive partitioning analysis classification tree using RTOG 0126 cohort data.

Figure 3. Kaplan-Meier estimates of overall survival stratified by RPA classification for (a) NRG/RTOG 0126 and (b) NRG/RTOG 9406.

Table 1. Demographic and disease characteristics.

	RTOG 0126 70.2 Gy (n=605)	RTOG 0126 79.2 Gy (n=597)	RTOG 9406 (n=864)	Total (n=2066)	p-value[1]
Age					0.001
Median	71	71	69	70	
Min - Max	33 - 86	49 - 87	41 - 85	33 - 87	
Q1 - Q3	64 - 74	65 - 74	64 - 73	64 - 74	
Race[2]		White vs black/African American vs. Other			<0.001
American Indian or Alaskan Native	2 (0.3%)	4 (0.7%)	2 (0.2%)	8 (0.4%)	
Asian	6 (1.0%)	7 (1.2%)	0 (0.0%)	13 (0.6%)	
Black or African American	69 (11.4%)	78 (13.1%)	142 (16.4%)	289 (14.0%)	
Native Hawaiian or Other Pacific Islander	0 (0.0%)	1 (0.2%)	10 (1.2%)	11 (0.5%)	
White	515 (85.1%)	492 (82.4%)	642 (74.3%)	1649 (79.8%)	
More than One race	2 (0.3%)	1 (0.2%)	0 (0.0%)	3 (0.1%)	
Other	0 (0.0%)	0 (0.0%)	10 (1.2%)	10 (0.5%)	
Unknown	11 (1.8%)	14 (2.3%)	58 (6.7%)	83 (4.0%)	
Ethnicity		Not Hispanic or Latino vs Hispanic or Latino/Other			0.054
Hispanic or Latino	19 (3.1%)	19 (3.2%)	57 (6.6%)	95 (4.6%)	
Not Hispanic or Latino	545 (90.1%)	543 (91.0%)	807 (93.4%)	1895 (91.7%)	
Unknown	41 (6.8%)	35 (5.9%)	0 (0.0%)	76 (3.7%)	
Comorbidity Score[3]	(n=602)	(n=596)	(n=864)	(n=2062)	<0.001
0	293 (48.7%)	275 (46.1%)	525 (60.8%)	1093 (53.0%)	
1-2	274 (45.5%)	291 (48.8%)	337 (39.0%)	902 (43.7%)	
3-5	35 (5.8%)	30 (5.0%)	2 (0.2%)	67 (3.2%)	
Gleason Score	(n=605)	(n=597)	(n=863)	(n=2065)	<0.001
2-6	101 (16.7%)	102 (17.1%)	484 (56.1%)	687 (33.3%)	
7	504 (83.3%)	495 (82.9%)	272 (31.5%)	1271 (61.5%)	
8-10	0 (0.0%)	0 (0.0%)	107 (12.4%)	107 (5.2%)	
PSA	(n=605)	(n=597)	(n=863)	(n=2065)	<0.001
Median	7.8	7.53	8.4	7.9	
Min - Max	0.1 - 19.9	0.3 - 19.7	0.1 - 69.5	0.1 - 69.5	
Q1 - Q3	5.41 - 10.78	5.26 - 10.9	5.6 - 12.8	5.4 - 11.34	
Induction ADT			(n=864)	(n=864)	NA
No	-	-	545 (63.1%)	545 (63.1%)	
Yes	-	-	319 (36.9%)	319 (36.9%)	
Weight			(n=815)	(n=815)	NA
Median	-	-	85.3	85.3	
Min - Max	-	-	53.1 - 188.3	53.1 - 188.3	
Q1 - Q3	-	-	76.4 - 95	76.4 - 95	

[1] Kruskal-Wallis test for continuous variables and Chi-square test for categorical variables

[2] In NRG/RTOG 9406 race and ethnicity were collected as one variable; patients reported as "Hispanic" are displayed in this table under "Ethnicity" and are marked as "Unknown" under "Race."

[3] Four patients in NRG/RTOG 0126 were missing the comorbidity form and do not have a calculated comorbidity score

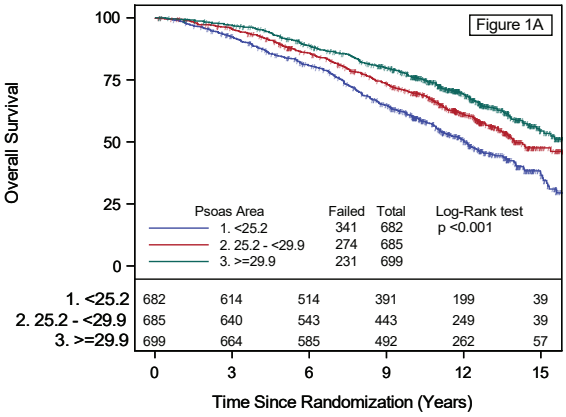
Table 2. Summary of body composition assessment.

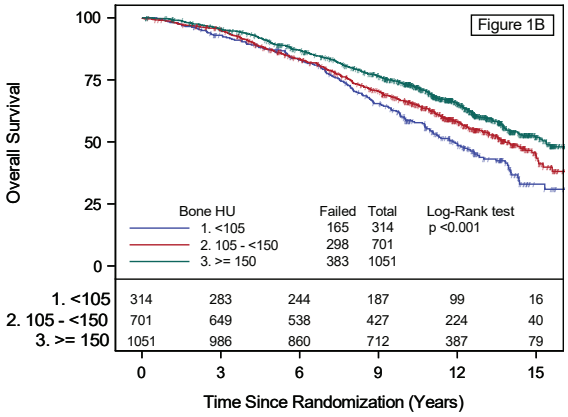
	RTOG 0126 70.2 Gy (n=605)	RTOG 0126 79.2 Gy (n=597)	RTOG 9406 (n=864)	Total (n=2066)	p-value[1]
PSOAS Area					0.249
Median	28.12	27.57	27.58	27.69	
Min - Max	12.98 - 52.3	10.23 - 44.93	9.48 - 57.97	9.48 - 57.97	
Q1 - Q3	24 - 31.62	24.37 - 31.4	23.235 - 31.16	23.8 - 31.34	
Psoas Area (cat.)					0.262
<25.2	191 (31.6%)	187 (31.3%)	304 (35.2%)	682 (33.0%)	
25.2 - <29.9	201 (33.2%)	215 (36.0%)	269 (31.1%)	685 (33.2%)	
>=29.9	213 (35.2%)	195 (32.7%)	291 (33.7%)	699 (33.8%)	
SM Area					<0.001
Median	142.64	140.67	135.35	139.015	
Min - Max	67.96 - 240.2	67.88 - 232.3	57.9 - 281.51	57.9 - 281.51	
Q1 - Q3	123.67 - 161.1	122.5 - 156.67	116.09 - 153.19	120.24 - 156.67	
Bone HU (cont.)					0.093
Median	146.76	150.82	155.22	151.36	
Min - Max	30.83 - 429.6	17.11 - 687.43	14.36 - 418.88	14.36 - 687.43	
Q1 - Q3	119.11 - 183.93	114.74 - 191.7	121.59 - 189.025	119.34 - 188.63	
Bone HU (cat.)					0.009
<105	102 (16.9%)	107 (17.9%)	105 (12.2%)	314 (15.2%)	
105 - <150	216 (35.7%)	189 (31.7%)	296 (34.3%)	701 (33.9%)	
≥ 150	287 (47.4%)	301 (50.4%)	463 (53.6%)	1051 (50.9%)	
Adipose HU (cont.)					<0.001
Median	-101.45	-102.41	-98.885	-100.96	
Min - Max	-145.87 - -57.5	-139.63 - -62.82	-158.65 - -55.2	-158.65 - -55.2	
Q1 - Q3	-112.77 - -95.8	-114.23 - -97.25	-108.11 - -92.995	-110.54 - -94.85	
Adipose HU (cat.)					<0.001
< -104	244 (40.3%)	261 (43.7%)	298 (34.5%)	803 (38.9%)	
-104 - < -99.5	121 (20.0%)	117 (19.6%)	115 (13.3%)	353 (17.1%)	
-99.5 - < -95	109 (18.0%)	108 (18.1%)	167 (19.3%)	384 (18.6%)	
≥ -95	131 (21.7%)	111 (18.6%)	284 (32.9%)	526 (25.5%)	
Psoas HU (cont)	(n=588)	(n=582)	(n=850)	(n=2020)	<0.001
Median	41.22	40.525	44.155	42.555	
Min - Max	-2.05 - 105.7	1.41 - 108.7	2.42 - 92.65	-2.05 - 108.7	
Q1 - Q3	28.755 - 48.835	27.58 - 48.45	35.08 - 50.66	31.295 - 49.375	
Psoas HU (cat)	(n=588)	(n=582)	(n=850)	(n=2020)	<0.001
<35.6	220 (37.4%)	225 (38.7%)	219 (25.8%)	664 (32.9%)	
35.6 - <46.9	190 (32.3%)	181 (31.1%)	300 (35.3%)	671 (33.2%)	
>=46.9	178 (30.3%)	176 (30.2%)	331 (38.9%)	685 (33.9%)	

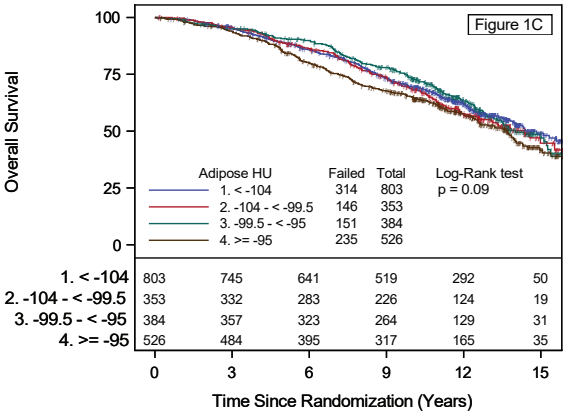
[1] Kruskal-Wallis test for continuous variables and Chi-square test for categorical variables

Table 3. Multivariable Cox proportional hazards model for overall survival with body composition variables as categorical variables (n=2061).

Parameter	Level	HR (95% CI)	p-value
Adipose HU	< -104	Ref	.
	-104 - < -99.5	1.089 (0.892, 1.331)	0.4017
	-99.5 - < -95	0.979 (0.8, 1.197)	0.8365
	≥ -95	1.165 (0.978, 1.387)	0.0864
Bone HU	<105	Ref	.
	105 - <150	0.942 (0.775, 1.145)	0.5479
	≥150	0.837 (0.688, 1.017)	0.0739
Psoas Area	<25.2	Ref	.
	25.2 - <29.9	0.787 (0.669, 0.926)	0.0040
	≥29.9	0.714 (0.599, 0.852)	0.0002
Treatment Group	9406	Ref	.
	0126 - 70.2 Gy	0.861 (0.709, 1.046)	0.1323
	0126 - 79.2 Gy	0.909 (0.751, 1.101)	0.3309
Age		1.055 (1.043, 1.068)	<.0001
Comorbidity Score	0	Ref	.
	1-2	1.54 (1.337, 1.773)	<.0001
	3-5	2.573 (1.876, 3.529)	<.0001
Baseline PSA		1.015 (1.004, 1.026)	0.0067
Gleason Score	2-6	Ref	.
	7	1.119 (0.947, 1.323)	0.1879
	8-10	0.904 (0.635, 1.287)	0.5764
Race	White	Ref	.
	American Indian or Alaskan Native	0.916 (0.339, 2.481)	0.8635
	Asian	0.716 (0.296, 1.732)	0.4584
	Black or African American	1.17 (0.941, 1.455)	0.1589
	Native Hawaiian or Other Pacific Islander	0.684 (0.219, 2.14)	0.5143
	Other	0.854 (0.581, 1.255)	0.4208







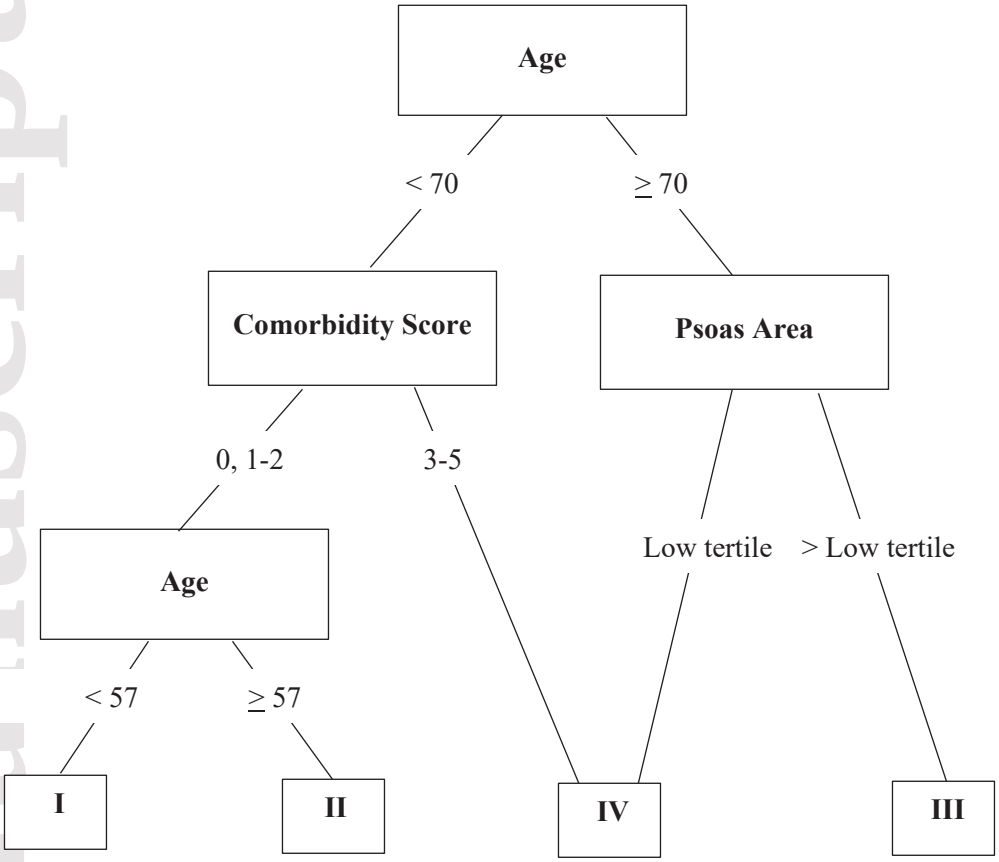


Figure 3A

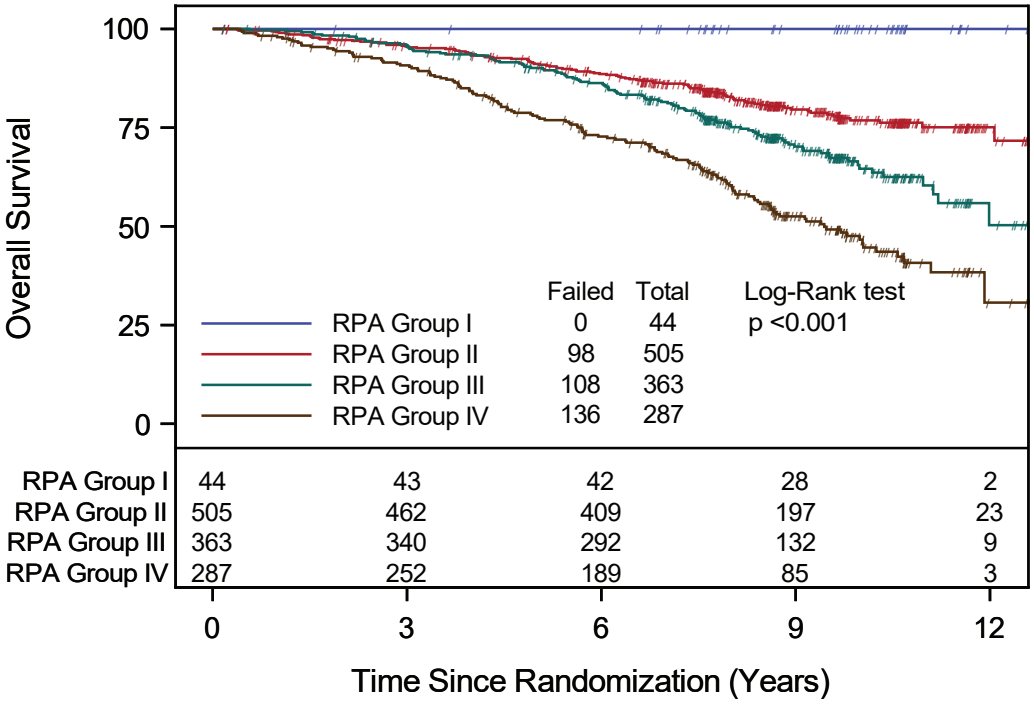


Figure 3B