ISSN (Print) 1226-1750
ISSN (Online) 2233-6656
Journal of Magnetics 24(4), 698-703 (2019) https://doi.org/10.4283/JMAG.2019.24.4.698

Visceral Obesity Assessment by MRI and Prostate Cancer Risk

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(Received 28 August 2019, Received in final form 20 October 2019, Accepted 21 October 2019)

The incidence of prostate cancer has gradually increased with obesity in Korean males. We aimed to quantify visceral fat content measured by magnetic resonance imaging (MRI) as a risk factor of prostate cancer. This case-control study that included 100 patients (mean age, 66.1 ± 7.1 years) newly diagnosed with prostate cancer and 100 healthy males (mean age, 63.4 ± 4.6 years) without cancer. All subjects underwent 3.0 Tesla MRI. Prostate cancer patients had a significantly higher abdominal fat ratio ($p < 0.04$) and regression for prevalence ($\beta = 0.52$, $p < 0.01$), other than obesity factors (waist circumference and body mass index), than the controls. In prostate cancer patients, a higher abdominal fat ratio was associated with a higher Gleason score level using odds ratios but excluding other obesity factors. Abdominal fat ratio is a risk factor of prostate cancer and clinical stage.

Keywords : MRI, visceral fat, body composition, obesity, Prostate cancer

1. Introduction

The incidence of prostate cancer has been increasing steadily in Korean males; this may be due to the increased popularity of the prostate-specific antigen (PSA) screening program [1]. Moreover, profound changes in the prostate cancer incidence in Korean males may reflect changes to a westernized lifestyle [2-6]. Although there is no clear evidence that a westernized lifestyle is associated with prostate cancer [6, 7], numerous studies have shown that obesity is related with prostate cancer development and progression [1, 6, 7]. In addition, recent studies have reported that obesity is associated with an increased risk of advanced prostate cancer compared with localized disease [2, 3], with mixed results [6-9]. The reason for these mixed results is the due to the variation in how obesity is assessed [7-10]. Another One reason for such disparate outcomes may be due to the use of simple anthropometric measurements, including weight and body mass index (BMI), which does not reflect individual body composition such as fat or muscle mass. Particularly in males with greater muscle mass, simple anthropometric measurement is not an appropriate obesity study method due to its imperfect reflection of body fat distribution [10-13]. However visceral adipose tissue [VAT] is assumed to be a more accurate assessment of obesity than BMI because it is high lipolytic active and release large amounts of free fatty acids metabolically active also turn outs carcinogenesis for risk of prostate cancer such as cytokines including tumor necrosis factor-α, interleukin-6,leptin, and adiponectin [10].

Therefore, obtaining cross-sectional body images can be used to quantify the visceral fat content using medical modalities such as magnetic resonance imaging (MRI).

We hypothesized that a higher visceral fat content measured by MRI could be associated with the incidence of prostate cancer as well as higher-grade disease. Therefore, this study aimed to examine the association between visceral fat content with prostate cancer incidence and tumor grade.

2. Populations and Methods

The study was approved by our facility's institutional review board, and written informed consent was obtained from all subjects.

The subjects visited one hospital in Korea from January 2 to December 20, 2017. To investigate the association

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between the visceral fat content measured by MRI and the risk of prostate cancer, the participants were divided into two groups: 1) newly diagnosed with prostate cancer patients (case group = 100) and 2) healthy males who were not diagnosed with any cancer (control group = 100). Patients who underwent systemic therapy, radiotherapy, or radical surgery for other cancers were excluded.

All subjects' profile information (height, weight, PSA, Gleason score [GS]) was obtained from electronic medical records. Individual weight and height measurements were collected at the time of clinic visit. Demographic information regarding educational level and family history were obtained with the use of questionnaires. The associations of obesity or visceral fat content with biopsy GS were evaluated.

Abdominal fat ratio was measured using MRI after the initial diagnosis of prostate cancer in the cases and during a regular health examination in the controls. All MRI examinations were performed on a 3.0 Tesla Achieva TX MR system (Philips Medical Systems, Best, The Netherlands) using a SENSE-XL-Torso imaging coil set on the abdomen. To determine the distribution of abdomen adiposity (VAT versus subcutaneous adipose tissue [SAT]), we used T2-weighted cross-sectional MRI at the umbilicus level to measure the diameter of the anterior abdominal musculature (A), posterior abdominal musculature (P), and anterior to posterior abdominal musculature (AP) in all subjects (Fig. 1). A and P were measured as the cross-sectional subcutaneous fat thickness between the skin and the A or the P. The SAT value is calculated using the formula $SAT = A+P$, and VAT is calculated using the formula $VAT\% = [(AP–SAT)/AP] \times 100$. This method was introduced by Qu [4, 5], but a number of relevant papers

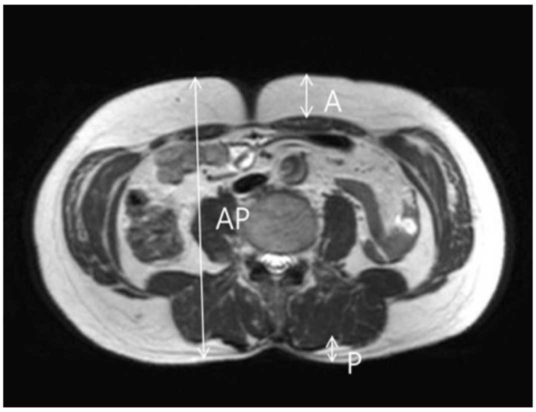

Fig. 1. Measurements of distributional abdominal adipose tissue from MRI. Measuring by MRI, A, P and AP were measured in three images around the umbilicus level. A, anterior abdominal fat; AP, anteroposterior diameter; P, posterior abdominal fat.

have reported this method, which is commonly used to assess the amount of adipose tissues [4, 5].

We performed randomly assigned by using a double-blind random allocation (blinded participant's information) with permuted duplication data assignments identified by other person.

The subjects' demographic characteristics were examined using t-test and chi-square analysis to determine significant differences. We performed multiple regression analysis to determine the effect of visceral fat content on prostate cancer risk and grade. Among the obesity factors relevant to prostate cancer, odds ratios (ORs) and 95 % confidence intervals (CIs) were analyzed by entered logistic regression. Continuous variables were divided into two groups by median during the logistic regression. The statistical analysis was performed using SPSS statistics v. 20 (SPSS Inc., Chicago, IL, USA), and p values < 0.05 were considered statistically significant.

3. Results

Table 1 shows the subjects' demographic characteristics. Mean age was 66.1 ± 7.1 years (range, 48-85 years) and 63.4 ± 4.6 (range, 48-85 years) in cases and controls, respectively. There were no statistically significant intergroup differences in age, family history of prostate cancer, education level, BMI, and waist circumference. Mean waist circumference and BMI was 86.5 cm and 24.7 in the case group and 83.7 cm and 24.3 in the control group. There was no intergroup difference in age, education level, family history, BMI, or waist circumference.

Figure 2 shows the abdominal fat ratios of the case and control groups (51.6 ± 7.9 and 49.4 ± 8.1, respectively). The prostate cancer patients had a moderately higher abdominal fat ratio ($p < 0.04$ for t-test) than the controls. Multiple regression analysis showed a positive association between abdominal fat ratio and the incidence of prostate cancer ($\beta = 0.52$, $r = 0.43$, $p < 0.01$) when all obtained variables (abdominal fat ratio, BMI, waist circumference, age, education level, and family history) were entered into the model.

To determine the ORs of the incidence of prostate cancer in all subjects, we performed a logistic regression analysis of obesity factors (waist circumference, BMI, abdominal fat ratio, and total fat) at the median cut-off points (1^{st} vs 2^{nd}) of 85.0 cm, 24.0, 51.5 %, and 21,500 mm^2, respectively. Table 2 shows the crude and adjusted ORs of prostate cancer risk in all subjects. Abdominal fat ratio had the greatest significant effect on the incidence of prostate cancer (OR and 95 % CI; 2.41 and 1.04-3.89, $p < 0.03$). Multiple regression analysis of abdominal fat ratio,

Table 1. Demographic characteristics of study participants.

		Case	Control	p-value
Age (Year)	< 60	17 (17 %)	19 (19 %)	0.51
	60-69	49 (49 %)	53 (53 %)	
	≥ 70	34 (34 %)	28 (28 %)	
Family history	Yes	3 (3 %)	1 (1 %)	0.71
	No	97 (97 %)	99 (99 %)	
Level of education	Under middle school	28 (28 %)	13 (13 %)	0.09
	Under high school	44 (44 %)	31 (31 %)	
	Over college	28 (28 %)	56 (56 %)	
Waist circumference (cm)	≤ 79.9	17 (17 %)	21 (21 %)	0.11
	80.0-89.9	62 (62 %)	63 (63 %)	
	≥ 90	21 (21 %)	16 (16 %)	
BMI	≤ 22.9	46 (46 %)	45 (45 %)	0.35
	23-27.4	49 (49 %)	52 (52 %)	
	≥ 27.5	5 (5 %)	3 (3 %)	
PSA (ng/ml)	≤ 9.9	49 (49 %)	No information due to no check for Control	
	10-19.9	16 (16 %)		
	≥ 20	35 (35 %)		
Gleason score	< 6	19	No information due to no check for Control	
	≥ 7	81		

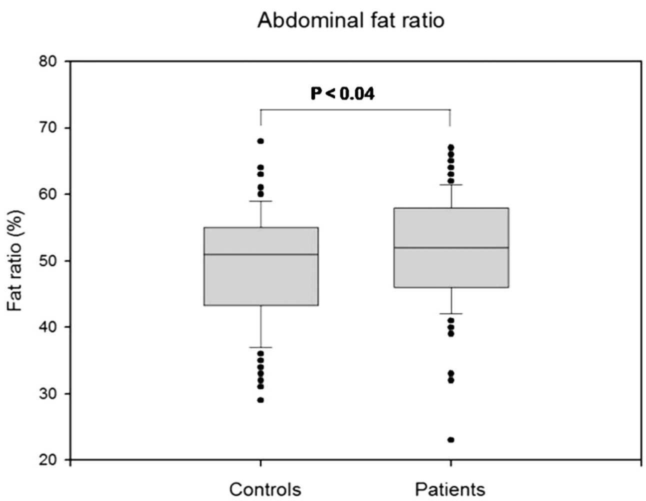

Fig. 2. Statistical differenced abdominal fat ratio diagram: comparison between prostate cancer patients and controls (normal participants). · Circles represent outliers.

BMI, waist circumference, and age revealed an association between predicting pathological stage of prostate cancer and obesity factor has shown similar with incidence of prostate cancer. Among the obesity factors, abdominal fat ratio ($\beta = 0.45$, $p < 0.04$) had the strongest positive association with GS. However, BMI ($\beta = 0.19$, $p < 0.16$) and aging ($\beta = 0.10$, $p < 0.04$) were less closely associated with GS.

To identify the association between each obesity factor and pathological stage in prostate cancer patients, GS was divided into two groups (6 and ≥ 7) and independent variables (abdominal total fat, BMI, abdominal fat ratio, and total fat) were divided into two groups by cutoff points (1^{st} vs 2^{nd}) of median 86.5 cm (waist circumference), 24.7 (BMI), 52.5 % (abdominal fat ratio), and 23,000 mm^2 (total fat), and a logistic regression analysis was performed. Table 3 shows the crude and adjusted ORs of the association between obesity factors and GS in prostate cancer patients when categorized as GS categorized as

Table 2. Odds ratios and 95 % CI on prostate cancer risk in relation to obesity in all of subjects.

Factors		Crude	p-value	Adjusted for age, education level, and family history	p-value
		Odds ratio (95 % CI)		Odds ratio (95 % CI)	
Waist-circumference (In)	1^{st} vs 2^{nd}	1.88 (0.25-2.01)	< 0.09	1.55 (0.19-2.07)	< 0.17
BMI	1^{st} vs 2^{nd}	1.03 (0.85-3.59)	< 0.41	0.93 (0.99-9.28)	< 0.52
Abdominal fat ratio (%)	1^{st} vs 2^{nd}	2.41 (1.04-3.89)	< 0.03	2.23 (1.05-3.93)	< 0.05
Total abdominal fat (mm^2)	1^{st} vs 2^{nd}	1.36 (0.46-4.07)	< 0.34	1.30 (0.37-4.60)	< 0.39

Table 3. Odds ratios and 95 % CI on Gleason score ≥ 7 risk in relation to obesity factors.

Factors		Crude	p-value	Adjusted for age, education level, and family history	p-value
		Odds ratio (95 % CI)		Odds ratio (95 % CI)	
Waist-circumference (In)	1st vs 2nd	1.73 (0.25-2.19)	< 0. 08	1.66 (0.19-2.28)	< 0. 12
BMI	1st vs 2nd	1.12 (1.02-3.87)	< 0.41	1.09 (1.23-10.65)	< 0.52
Abdominal fat ratio (%)	1st vs 2nd	3.01 (1.18-8.80)	< 0.05	2.81 (1.16-9.76)	< 0. 10
Total abdominal fat (mm^2)	1st vs 2nd	1.36 (0.46-4.07)	< 0.20	1.30 (0.37-4.60)	< 0.35

< 6 and ≥ 7 in prostate cancer patients. Among the obesity factors, abdominal fat ratio was the most closely associated with GS level. The higher abdominal fat ratio group showed a higher GS level (≥ 7) than the lower abdominal fat ratio group (6 <) (OR and 95 % CI; 3.01 and 1.18-8.80, $p < 0.05$). Among the obesity factors, BMI had the weakest association with GS level (OR and 95 % CI; 1.12 and 1.02-3.87, $p < 0.41$).

4. Discussion

These data showed differences between prostate cancer patients and healthy individuals who visited our specialized cancer institute. Our results support the hypothesis that a higher distribution of abdominal visceral fat is useful for predicting the clinical outcome the development of prostate cancer into higher-grade cancer. Not long ago, the incidence of prostate cancer was relatively very low in South Korea, but it has increased steadily than that of other major cancers in males recently from 2000 years [12].

According to the Korea National Health and Nutrition Examination Survey, the eating patterns of Koreans changed from the traditional Korean diet (high vegetable, low animal fat intake) to a substantially westernized diet (low vegetable, high animal fat intake); therefore total energy intake increased from 948.3 kcal in 1998 to 1,063.2 kcal in 2012. During this same period, the proportions of protein and carbohydrate intakes increased to 12.3 % and 3.0 %, respectively, whereas that of animal fat in 2012 was increased to 20.5 % [11, 12].

There is good evidence that the Western diet plays a significant role in the risk of prostate cancer obtained from an immigrant study in which Asian-American men living in the United States have much a higher incidence (50 per 100,000 man-years) than do those in their native counties (10-20 per 100,000 man-years) [4]. Compared to the 1970s, in countries with a low incidence of prostate cancer (Asian countries), the reason for the increased incidence of prostate cancer in recent years is related to the westernized lifestyle [1]. Adoption of a Western lifestyle has led to obesity resulting from the influence of a high intake of fast food and junk food, a low intake of vegetables, and very low physical activity.

Our results demonstrate that prostate cancer patients have more visceral fat than age-matched controls, which supports the results of previous related studies in which the incidence of prostate cancer increased with abdominal visceral fat content [14]. That is, accumulated visceral fat plays a role in prostate cancer risk. Adipose tissue is influenced by adiponectin, resistin, leptin, and adipsin and directly related to C-reactive protein, tumor necrosis factor-α, and interleukin-6 levels. Generally, levels of these specific hormones are lower in obese than in lean men; insulin resistance is correlated with human obesity [15, 16]. Finally, these higher hormone levels lead to an elevated risk of prostate cancer and poor clinical stage.

A previous study that estimated distribution of abdominal fat showed that prostate cancer patients had a significantly higher visceral fat (OR, 4.6) [14]. In accordance with that previous study, we also found a positive association between visceral fat content and prostate cancer risk.

We found that, in prostate cancer patients, waist circumference was not associated with GS but had a strong positive association with abdominal fat ratio. Our multiple regression analysis of the association between predicting GS (pathological stage) of prostate cancer and obesity factors showed a similar incidence of prostate cancer. Therefore, we suggest that the abdominal fat ratio obtained on MRI images is a good biomarker for prostate cancer risk and GS.

Several processes can explain the effect of the accumulation of visceral fat. Visceral fat is metabolically active tissue that secretes a variety of hormones and cytokines (testosterone, estrogen, sex hormone-binding globulin, insulin, insulin-like growth factor-1, insulin-like growth factor binding protein [IGFBP], interleukin-6, leptin, and adiponectin) that affect prostate cancer [14]. There is evidence that a visceral fat accumulation is associated with insulin resistance, resulting in hyper-insulinemia. A high caloric intake promotes the increased high plasma and decreased levels of IGFBP-1 and -2. Increased insulin and decreased levels of IGFBP-1 and -2 can lead to the development of several different cell lines, such as prostate cancer, specifically in cases of early diagnosed prostate cancer [17-19].

In prostate cancer patients, PSA levels and GS are used to predict pathological stage. A recent study suggested that PSA level was slightly lower among obese men than slim men [18]. Because PSA level is regulated by androgens, lower PSA levels may result from decreased androgenic activity in obese men [20]. Our results also demonstrated that PSA levels are lower, although overweight or obese men had larger prostates than non-obese men.

Positive family history of prostate cancer is a known risk factor. Men with a first-degree family history (brother or father) have a 2- to 4-fold increased risk of prostate cancer and higher GS [21]. Only one man in the current study had a family history of prostate cancer. That reason, prostate cancer is an unprecedented disease in Korea due to a lack of knowledge about the relatively old patients' family members with prostate cancer. Thus, an analysis of family history in this study was impossible analysis.

The 77 prostate cancer patients in our study had no other cancers, but 4 had tuberculosis, 12 had hypertension, 6 had diabetes, and 1 had myocardial infarction.

Although the number of subjects was too small to prove the association between prostate cancer and visceral fat content, we believe that our results are valuable since they can at least partially explain the incidence of prostate cancer in Korea.

This study has the limitation of not proving the association between prostate cancer and visceral fat content due to the small total number of subjects (especially for case). a number of subjects was low due to the fact that our included prostate cancer patients could not complete any cancer treatment (chemotherapy, radiation therapy, and surgery) after visiting the hospital during the study period. However, this study shows a significant association of visceral fat content with the risk of prostate cancer.

5. Conclusion

A higher visceral fat content was observed in prostate cancer patients than in the controls and showed a stronger association with the risk of prostate cancer than conventional anthropometric measurements (waist circumference and BMI) for obesity as a risk factor for prostate cancer. Visceral fat content can be considered a candidate biomarker for prostate cancer.

Acknowledgements

This study was supported by a Korean National Cancer Center Grant, No. 1810021.

References

[1] S. Rebecca, M. Jiemin, Z. Zhaohui, and J. Ahmedin, CA Cancer J. Clin. **64**, 9 (2014).

[2] C. Rodriguez, A. V. Patel, E. E. Calle, E. J. Jacobs, A. Chao, and M. J. Yhun, Cancer Epidemiol. Biomark. Prev. **10**, 345 (2001).

[3] E. E. Calle, C. Rodriquez, K. Walker-Thurmond, and M. J. Thun, N Engl. J. Med. **348**, 1625 (2003).

[4] Y. Y. Qu, B. Dai, Y. Y. Kong, K. Chang, D. W. Ye, X. D. Yao, S. L. Zhang, H. L. Zhang, and W. L. Yang, Asian J. Androl. **15**, 747 (2013).

[5] P. Mucksavage, C. Mitchell, A.Kutikov, A. J. Wein, D. Torigian, and S. B. Malkowicz, UrolOncol **30**, 595 (2012).

[6] Ministry of Health and Welfare, Korea Centers for Disease Control & Prevention. National Health Statics. The Fourth Korean National Health and Nutrition Examination Survey. 2007. Korean Ministry of Health and Welfare, Seoul.

[7] C. Rodriguez, S. J. Freedland, A. Deka, E. J. Jacobs, M. L. McCullough, A. V. Patel, M. J. Thun, and E. E. Calle, Cancer Epidemiol Biomarkers Prev. **16**, 63 (2007).

[8] J. G. van Roermund, D. E. Kok, M. F. Wildhagen, L. A. Kiemeney, F. Struik, S. Sloot, I. M. van Oort, C. A. Hulsbergen0van de Kaa, G. J. van Leenders, C. H. Bangma, and J. A. Witjes, BJU Int. **104**, 321 (2009).

[9] J. G van Roermund, K. A. Hinnen, J. J. Battermann, J. A. Witjes, J. L. Bosch, L. A. Kiemeney, and M. van Vulpen, BJU Int. **105**, 42 (2009).

[10] W. P. Tan, C. Lin, M. Chen, and L. A. Deane, Urology **98**, 107 (2016).

[11] Ministry of Health and Welfare, Korea Centers for Disease Control & Prevention. National Health Statics.The Fourth Korean National Health and Nutrition Examination Survey. 2010. Korean Ministry of Health and Welfare, Seoul.

[12] Korean National Cancer Information Center. 2014. Annual report of cancer statics in Korea in 2012. Republic of Korea.

[13] T. Weits, E. J. van der Beek, M. Wedel, and B. M. Ter-HaarRomeny, Int. J. Obesity **12**, 217 (1998).

[14] P. vonHafe, F. Pina, A. Perez, M. Tavares, H. Barros, Obes. Res. **1**, 1930 (2004).

[15] I. Kelesidis, T. Kelesidis, and C. S. Mantzoros, Br. J. Cancer **94**, 1221 (2006).

[16] W. H. Chung, Korean J Urol. **50**, 540 (2006).

[17] P. L. Grover and F. LMartinL, Carcinogenesis **23**, 1095 (2002).

[18] P. Stattin, A. Bylund, S. Rinaldi, C. Biessy, H. Déchaud, U. H. Stenman, L. Egevad, E. Riboli, G. Hallmans, and R. Kaaks, J. Natl. Cancer Inst. **92**, 1910 (2009).

[19] J. Baillargeon, B. H. Pollock, A. R. Kristal, P. Bradshaw,

J. Hernandez, J. Basler, B. Higgins, S. Lych, T. Rozanski, D. Troyer, and I. Thompson, Cancer **103**, 1092 (2005).
[20] S. J. Freedland and E. A. Platz, Epidemiol. Rev. **29**, 88 (2007).
[21] J. R. Bloom, S. L. Stewart, I. Oakley Girvan, P. J. Banks, and S. Chang, Cancer Epidemiol Biomarkers Prev. **15**, 2167 (2006).