Current Science International Volume : 07 | Issue : 04| Oct.- Dec. | 2018
ISSN: 2077-4435 Pages: 818-825

Obesity is a Predictor of Prognosis Lung Cancer Follow Up by PET/CT

Omar H. Omar[1], Safenaz Y. El Sherity[2] and Yehia O. Hussein[3]

[1]*Radiology Department, Faculty of Medicine, Ain shams University, Cairo, Egypt.*
[2]*Biological Anthropology Department, Medical Research Division, National Research Centre (NRC), Dokki, Giza, Egypt (Affiliation ID 60014618).*
[3]*PET/CT Department, Misr Radiology Center, Cairo, Egypt.*

Received: 30 Sept. 2018 / Accepted: 19 Dec. 2018/ Publication date: 30 Dec. 2018

ABSTRACT

Background: Lung cancer is one of the commonest cancer and obesity considers one of non-communicable major health problem. The association between them is an important issue to study. Positron emission tomography/computed tomography (PET/CT) is the most accurate molecular imaging modality to evaluate the prognosis after treatment. ***Objectives:*** To assess therapeutic responses of lung cancer by PET/CT and study its association with obesity to use as a predictor for lung cancer prognosis laterally. ***Methods:*** A cross-sectional prospective study, 120 patients were involved for follow up of lung cancer examined by PET/CT then compared to the previous scan, although obesity was assessed by anthropometric measurements; weight& height to calculate body mass index (BMI) and waist (WC) & hip circumferences (HC) to calculate Waist/hip ratio (WHR). ***Results:*** 41 of participants (34.2%) were obese, 39 (32.5 %) were overweight and 40 (33.3%) were of normal weight. Regarding the response of treatment; 29.2% had progressive course, 18.3% had stationary course, 40.8% had a partial regressive course and (11.7%) had complete regressive course. Additionally, there was a significantly positive correlation between increasing BMI and stationary & regressive courses, as well negative correlation with a progressive course ($P<0.05$). Moreover, WC and WHR had a positive significant correlation with progressive and stationary courses and negative correlation with a regressive course ($P<0.05$). ***Conclusion:*** Obesity is a good predictor for lung cancer prognosis during follow up therapeutic effect, particularly abdominal obesity especially waist circumference, as the obese patient had a good prognosis of treatment especially whose had less WC.

Keywords: obesity, lung cancer, predictor, prognosis and PET/CT

Introduction

Lung cancer worldwide considers the commonest cancer; its incidence is 11.6% and its mortality is 18.4% of total cancer-associated death (Rebecca et al., 2018). In Egypt, it represents 8.2% regarding the program of the national cancer institute (Ibrahim et al., 2014). Regarding the histopathological type of lung cancer, non-small cell lung cancer (NSCLC) accounted for about 85% (Ramalingam *et al.,* 2011). The standard treatment of this commonest type is chemotherapy associated with radiotherapy. Thus the evaluation of the therapeutic response is important to avoid toxic effect of ineffective chemotherapy and elevate 5 years survival rate, as it is accounted for 17.4% (Spiro and Silvestri, 2005). So, positron emission tomography/computed tomography (PET/CT) is the best non-invasive imaging modality for evaluating the therapeutic response and staging to detect the viable cells and changes occurred regarding size and metabolic activity (Mac *et al*., 2003) and (Novello *et al*., 2013).

Obesity and particularly abdominal adiposity had an association with increased risk of cancer incidence. Several studies reported that with different types of cancers (Chen *et al*., 2016), (Ma *et al*., 2013), (Aune *et al*., 2015) and (Wang *et al*., 2014). While other studies found an inverse relation between lung cancer and high body mass index (BMI) (Yang *et al*., 2013) and (Duan *et al*., 2015).

General obesity could be assessed by BMI, while abdominal obesity which reflects fat distribution in the abdominal region assessed by waist circumference (WC) and waist-hip ratio (WHR) (Hidayat *et al*., 2016). Previous researchers studied the association between obesity and

Corresponding Author: Safenaz Y. El Sherity, Biological Anthropology Dept., Medical Research Division, National Research Centre (NRC) and Medical Research Centre of Excellence (MRCE), Giza, Egypt. E-mail: dr_safy_youssif@yahoo.com

incidence of lung cancer, without giving any consideration about the prognosis of the disease during treatment, is it affected by obesity generally or abdominally or not.

Therefore we conducted this study for the following objectives, assess therapeutic responses of lung cancer by PET/CT and study its association with obesity generally and abdominally to find the relation between both, which can be used laterally as a predictor for lung cancer prognosis.

Patients and Methods

Participants:

A prospective study included one hundred and twenty patients (76 males and 44 females) examined for follow up lung cancer after chemotherapy, they referred from clinical oncologists to assess the response of therapy; their ages between 42 and 76 years. The inclusion criteria: those had a good general condition, pathologically proven bronchogenic carcinoma and finished appropriate therapy 4-6 months ago (chemotherapy for metastatic deposits and/or radiofrequency of primary lung lesion). The Exclusion criteria: those had impaired renal function, previous allergic reaction to intravenous contrast medium and a blood glucose level more than 200 mg/dl at the time of the examination. The current study was approved by the research ethics committee, faculty of medicine, Ain Shams University and each patient signed the informed written consent. This study was conducted between October 2017 and August 2018, at the Misr Radiology center (MRC), Cairo, Egypt.

Methods

- **Preparation of the Patient**: Fasting six hours before the examination, while 24 hours before assessment allow high protein and low carbohydrate diets with liquids, as well avoid smoking and caffeine.
- **The examination day:** Complete history from the patient (included the duration from the last session of chemotherapy& radiofrequency) and previous PET/CT scan to follow up were taken. Then fasting blood sugar was measured to start examination if (<200 mg/dl).
- **Obesity assessment:** Anthropometric measurements were taken according to International Biological Program recommendations (Hiernaux and Tanner 1969), as following; body weight was measured using scale balance with no shoes and light clothes, while the height was measured by a Holtain anthropometer. The waist and hip circumferences were measured (WC& HC), using a tape horizontally positioned just above the iliac crest exactly under umbilicus and at the largest circumference of buttocks respectively. Then, body mass index (BMI) and waist-hip ratio (WHR) were calculated; as body weight/ height in meter squared (Kg/m^2) and waist/hip circumferences respectively. Then, the patients were divided into 3 groups according to their BMI; the normal weight group (whose BMI 18.5 - 24.9 kg/m2), The overweight group (whose BMI 25 - 29.9 kg/m2) and the obese group (whose BMI was ≥ 30 kg/m2) (WHO, 2016).
- **PET/CT Technique**: 18F-fluorodeoxyglucose (18F-FDG) was injected intravenous 45-60 minutes before starting the scan, with an average dose 5-10 mCi for adults (0.1 mCi/ Kg). Then PET/ CT scan was done as the following using 128 slices Phillips Ingenuity TF, (Cleveland, OH, USA); non-contrast CT with low-dose for attenuation correction, then PET scan was taken from the skull to the mid-thigh, followed by post-contrast diagnostic CT with an injection of non-ionic contrast medium. Those sequences of three scans were sent to advanced work station to assess qualitatively (in combined PET and CT scans at axial, coronal and sagittal views) and quantitatively for measuring maximum standardized uptake value (SUVmax) of pathologic tracer accumulation at the primary lung cancer lesion and metastatic deposits.
- Finally, a comparison was done with previous PET/ CT scan to assess therapeutic response according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria (Zhao *et al*., 2018);
  - Progressive disease (PD): increased of tumor uptake peak SUVmax by at least 25%, or an appearance of new or more lesions.
  - Stationary disease (SD): no significant changes, almost same (increased < 25% or decreased < 30%).

- Partial response (PR): reduced of tumor uptake peak SUVmax by at least a 30%.
- Complete response (CR): complete disappearance of FDG uptake at the tumor lesion with no new FDG avid lesion (figure 1).

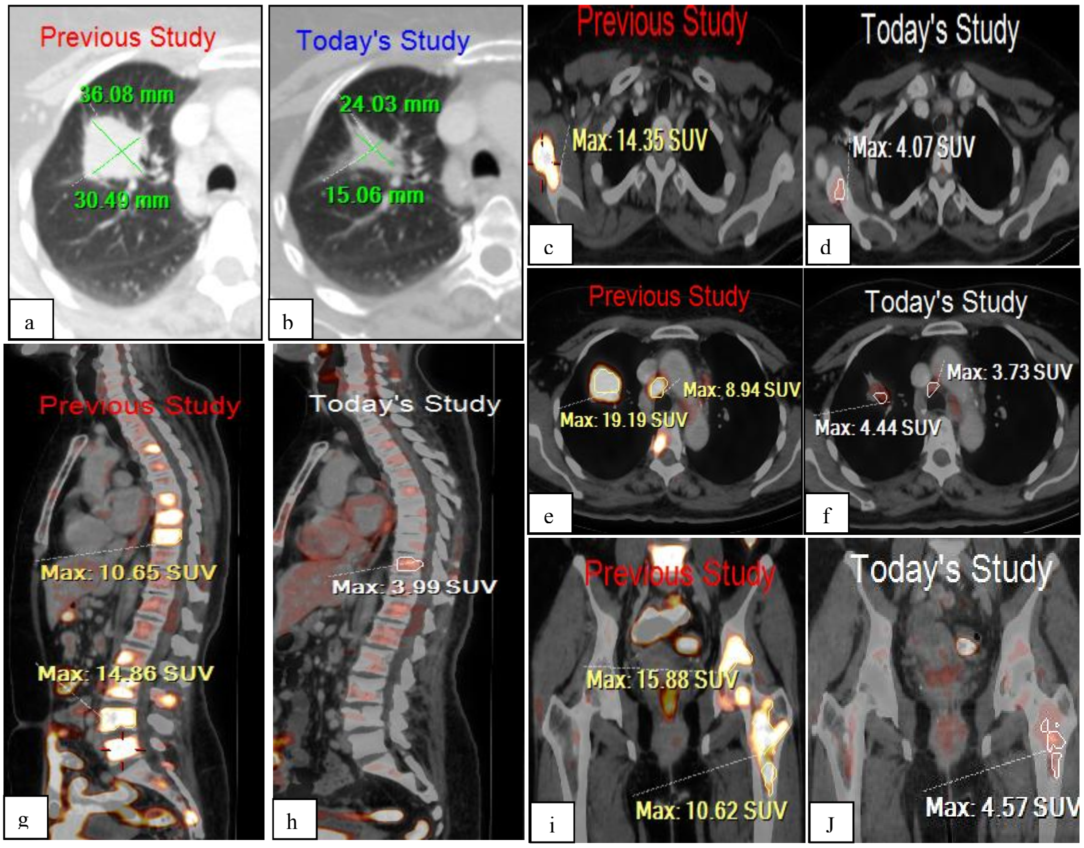

Fig. 1: Follow up of 66 years old female patient has metastatic right upper lung lobe cancer and received chemotherapy; revealed good therapeutic response in the form of marked regression as the following; (a & b) axial CT images of the lung window show morphological reduction of the primary lesion size measuring 24X15mm compared to 36X30mm (previously), (c & d) axial CT images show significant reduction of the right hypermetabolic glenoid osseous lesion measuring (SUV max 4.07 compared to 14.3), (e & f) axial combined PET/CT images show metabolically reduced of the previously noted right lung lesion and retro-caval lymph node, achieving SUVmax 4.4 and 3.7 (compared to SUVmax 19.19 and 8.94 previously) respectively, (g & h) sagittal PET/CT images show almost no metabolically uptake of vertebral osseous lesions in recent image (previously 14.8 SUVmax) apart from faint metabolic uptake at D10 vertebral body (SUVmax 3.9 compared to 10.6) and (i & J) coronal PET/CT images show faint metabolically uptake of the left sub-trochnatric osseous lesion in recent image (SUVmax 4.5 compared to 10.6).

Statistical Analysis

SPSS program was used to analyze the data (version 22, IBM Corporation); mean and standard deviations (SD) for parametric data, as well non-parametric data expressed their frequency distribution by numbers (percentage), one-way ANOVA, Pearson´s correlation and linear regression tests were done between variables. A statistical significance when $P < 0.05$.

Results

The current study included 120 patients had lung cancer; 76 males (63.3%) and 44 females (36.7%), their ages (42-76 years), anthropometric variables mean ± SD for both sex (males and females respectively) were done; age (62 ± 6.5 years & 56.5 ± 4.3 years), weight (76.8 ± 7.8 kg &

75.1 ± 6.9 kg), height (164.8 ± 2.9 cm & 163.9 ± 4.9 cm), BMI (28.2 ± 5.1 kg/m^2& 27.9 ± 5.4 kg/m^2), WC (87.6 ± 9.5 cm & 98.7 ± 7.1 cm), HC (105.9 ± 9.7 cm &113.8 ± 7.9 cm) and WHR (0.83 ± 0.05 & 0.87 ± 0.03). Regarding BMI; 40 (33.3%) were of normal weight (25 males and 15 females), 39 (32.5 %) were overweight (24 males and 15 females) and 41(34.2%) were obese (27 males and 14 females).

Regarding anthropometric parameters and BMI classification, obese patients with lung cancer had a significantly higher weight, BMI and WC at both sex (P<0.05), while statistically insignificant with height, HC and WHR (table 1).

Regarding the response of treatment during follow up lung cancer, the frequency distribution was done according to BMI (table 2). This depends on maximum 18 F-FDG uptakes on the primary lung lesion measuring by (SUVmax), as well avidity of metastatic deposits which compared to the previously examined PET/CT scan. The progressive course was detected in 35 patients (29.2%), 18 of those had normal weight. While 22 patients had a stationary course of the disease (18.3%), 50 % of those were obese (11 patients). Additionally, 49 patients (40.8%) had partial regression course (20 patients were obese, 17 were overweight and 12 were within normal weight). Moreover, complete regression course was recorded at 14 patients (11.7%); obese (7), overweight (4) and normal weight (3).

Table 1: Anthropometric parameters of normal weight, overweight and obese lung cancer patients at both sex

		Normal weight mean ±SD	Overweight mean ±SD	Obese mean ±SD	*P*-value
Weight (Kg)	Male	60.8± 3.4	77.2±4.8	91.3±3.1	0.00*
	Female	59.3±5.3	79.2±6.6	87.6±5.1	0.00*
Height(cm)	Male	163.1±4.4	168.8±5.2	163.7±4.9	0.07
	Female	163.1±7.9	167.1±4.5	160.3±4.4	0.17
BMI (Kg/m^2)	Male	22.7±1.6	27.4±1.5	34.0±2.6	0.00*
	Female	22.2±1.8	27.9±1.9	33.9±3.3	0.00*
WC (cm)	Male	84.2±6.7	86.1±7.4	92.9±6.8	0.02*
	Female	97.5±5.1	97.5±5.1	101.2±6.9	0.03*
HC (cm)	Male	101.6±5.0	103.92±6.2	112.7±7.7	0.12
	Female	113.2±6.7	115.20±6.4	117.1±8.6	0.55
WHR	Male	0.82±.04	0.83±.05	0.83±.05	0.66
	Female	0.86±.03	0.86±.04	0.87±.03	0.19

*Significant (P<0.05)

Table 2: Frequency distribution of treatment response in normal weight, overweight and obese lung cancer patients

	Total patients No. (%)	Normal Weight No. (%)	Overweight No. (%)	Obese No. (%)
Progression	35(29.2%)	18 (15%)	9 (7.5%)	8(6.7%)
Stationary course	22(18.3%)	5 (4.2%)	6 (5%)	11 (9.1%)
Partial regression	49(40.8%)	12(10%)	17(14.1%)	20(16.7%)
Complete regression	14(11.7%)	3(2.5%)	4 (3.3%)	7 (5.8%)

Then comparison was done between anthropometric parameters and response of lung cancer treatment at both sex; progressive, stationary and regressive (included both complete and partial response) courses, revealed that increased in WC and WHR were statistically significant associated with progressive course of lung cancer at both sex (P<0.05), additionally HC was significantly increased with females had progressive course (P<0.05) (table 3).

Regarding correlations between the response of treatment and anthropometric parameters, BMI had a positive significant correlation with stationary & regressive courses and significant negative correlation with a progressive course (P<0.05). Then controlling effect of BMI was done, found that the WC and WHR had a positive significant correlation with progressive and stationary courses and negative significant correlation with a regressive course of lung cancer (P<0.05). HC showed no significant correlation with a response of treatment (P>0.05) (table 4).

Finally, linear regression was done to predict the response of treatment of lung cancer by anthropometric parameters, revealed that WC is a predictor of prognosis lung cancer (P<0.05) (table 5).

Table 3: Comparison between the response of treatment and anthropometric parameters in lung cancer at both sex

	Sex	Progressive course No. (35) mean ±SD	Stationary course No. (22) mean ±SD	Regressive course No. (63) mean ±SD	*p*-value
BMI	Male	27.0±5.3	28.8±4.6	28.1±5.3	0.709
	Female	27.5±5.2	29.5±6.1	29.4±6.1	0.347
WC	Male	98.3± 5.4	87.9± 5.7	85.7±4.9	0.051*
	Female	104.1±5.9	97.0±6.4	94.4± 6.9	0.015*
HC	Male	107.1±6.9	105.8± 4.8	104.6± 6.4	0.679
	Female	120.12±6.7	112.5± 7.7	108.0±6.8	0.014*
WHR	Male	0.85±0.05	0.78±0.04	0.83± 0.05	0.041*
	Female	0.89±0.05	0.87±0.02	0.83± 0.04	0.980*

*significant (P<0.05)

Table 4: Correlations between the response of treatment and anthropometric parameters in lung cancer

		Progressive course	Stationary course	Regressive course
BMI	*r*	-0.784*	-0.746*	0.716*
	p	0.001	0.051	0.004
WC	*r*	0.771*	0.760*	-0.722*
	p	0.000	0.002	0.004
HC	*r*	0.191	0.352	0.365
	p	0.456	0.092	0.105
WHR	*r*	0.608*	0.725*	-0.756*
	p	0.000	0.051	0.000

r: correlation coefficient, * Significant at the level 0.05 or less

Table 5: Linear regression coefficients to predict the response of treatment of lung cancer by anthropometric parameters

Dependent variables	Standardized Coefficients Beta	R-Square	95% Confidence Interval for B Lower Bound	Upper Bound	F	*p*-value
BMI	-0.035	0.001	-1.295	0.882	0.14	0.708
WC	0.187	0.035	.087	4.275	4.25	0.041
WHR	0.148	0.022	-.002	0.018	2.65	0.106

Discussion

Obesity and related cancers are important health problems which increased rapidly worldwide. As, increased BMI (overweight and obese) consider a risk factor for different types of cancers like; colon, endometrium, pancreas, prostate, kidney and gall bladder (Renehan and Soerjomataram, 2016). While lung cancer not involved in the previously cancer-related list so it is interesting issue needs to study, particularly abdominal obesity and its association to lung cancer which couldn't be understood clearly. Abdominal obesity reflects those had higher waist circumference (WC) and waist to hip ratio (WHR) relative to others with the same BMI (Dewi *et al*., 2016).

Therefore, in this research we objective to study this relation in a different way, which is evaluate the association between therapeutic responses of lung cancer and obesity using the most accurate advanced sensitive imaging techniques, 18F-FDG PET /CT to assess the prognosis of the disease and its relation to obesity generally and abdominally. The most advantage of PET /CT is the detection of the metabolic changes (active viable cell) earlier than anatomical changes (tumor size) (Novello *et al*., 2013) and (Sheikhbahaei *et al*., 2017).

Regarding anthropometric measurements, the current study showed that obese patients with lung cancer (34.2%) had a significantly higher weight, BMI and WC at both sex. These findings were consistent with some researchers studied the relation between obesity and lung cancer, which revealed that inverse association between increased incidence of lung cancer with increasing BMI (Duan *et al*., 2015) and (Hidayat, 2016). Furthermore, many cohort prospective studies found a positive association between increased incidence of lung cancer and high WC and/or WHR after adjusted BMI (this adjusted reflects abdominal obesity while unadjusted reflects general obesity) (Dewi *et al*., 2016), (Olson *et al*., 2002), (Lam *et al*., 2013), (Renehan *et al*., 2008) and (Kabat *et al*., 2008). Moreover Leitzmann *et al.,* (2011), who reported a positive association between mortality from lung cancer and higher WC.

As, lung cancer cells have receptors for steroid hormones involved estrogens and androgens (Marquez-Garban, 2011), several biological mechanisms could be explained its association to obesity as; hyperinsulinemia, increased insulin-like growth factors I (IGF-I), reduced levels of sex hormone-binding globulin and increased levels of unbound hormones (androgens and estrogens) (Drinkard, 1995), (Olson, 2002), (Lam, 2013) and (Ankrapp, 1993). All of these mechanisms are strongly related to abdominal obesity rather total obesity (Hidayat, 2016).

Regarding correlations between the response of treatment and anthropometric parameters, the current study showed that increasing BMI was significantly associated with stationary & regressive courses (partially or complete). While increased WC and WHR were significantly associated with a progressive course of lung cancer at both sex, additionally increased HC within females. Thus, our findings suggest that increased abdominal fat tissue, not all body fatness, could be a good predictor for lung cancer prognosis. A meta-analysis study on six prospective researches to evaluate the association between lung cancer risk and obesity especially abdominal was done by Hidayat *et al*., (2016), who found that 10 cm increasing of WC was associated with high incidence of lung cancer risk by 10%, while this incidence was 5% with increasing WHR by 0.1. This positive association also was confirmed by several studies especially after adjusted BMI; (Kabat *et al*., 2008), (Dewi *et al*., 2016) and (Olson *et al.*, 2002).

Also, Janssen *et al.,* (2002) confirmed that WC after adjustment of BMI was better than WHR to predicate abdominal obesity. This may be due to the difficult interpretation of WHR, as a person may have abundant gluteal fat with low abdominal fat.

Strengths of the current study, it is the first research done to find the association between lung cancer prognosis after therapy and obesity which may be used in future to predict the outcome, also used PET/CT in follow up lung cancer patients, which is the most accurate radiological technique. While its limitation needs further longitudinal studies to determine the cutoff values of WC and WHR at which predict the prognosis of lung cancer after therapy.

In conclusion, obesity is a good predictor for lung cancer prognosis during follow up the therapeutic effect by PET/CT, particularly abdominal obesity especially waist circumference, as the obese patient had a good prognosis of treatment especially whose had less WC.

Conflict of interest

No conflict of interest was associated with the current study.

Acknowledgements

Authors are acknowledging all patients participated in the current study.

Author contribution

Omar H. Omar: gave conceptual advice, Safenaz Y. El Sherity (corresponding author): Analysis, interpretation the data, drafting the work and wrote the manuscript. Yehia O. Hussein: Acquisition of the data. All authors shared in design the work and approval of the final version to be published.

References

Ankrapp, D. and D. Bevan, 1993. Insulin-like growth factor I and human fibroblast-derived insulin-like growth factor-I stimulate the proliferation of human lung carcinoma cells in vitro. *Cancer Res.* 1993, *53*; 3399–3404.

Aune, D., D. Navarro Rosenblatt, D. Chan, S. Vingeliene, L. Abar, A. Vieira, D. Greenwood, E. Bandera and T. Norat, 2015. Anthropometric factors and endometrial cancer risk: A systematic review and dose-response meta-analysis of prospective studies. Ann. Oncol., 26, 1635–1648.

Chen, G., S. Chen, R. Zhang, K. Hidayat, J. Qin, Y. Zhang and L. Qin, 2016. Central obesity and risks of pre- and postmenopausal breast cancer: A dose-response meta-analysis of prospective studies. Obes. Rev., 17, 1167–1177.

Dewi, N., H. Boshuizen, M. Johansson, P. Vineis, E. Kampman, A. Steffen, A. Tjønneland, J. Halkjær, K. Overvad, G. Severi, et al., 2016. Anthropometry and the Risk of Lung Cancer in EPIC. Am. J. Epidemiol., 184, 129–139.

Drinkard, C., T. Sellers, J. Potter, W. Zheng, R. Bostick, C. Nelson and A. Folsom, 1995. Association of body mass index and body fat distribution with risk of lung cancer in older women. Am. J. Epidemiol., 142, 600–607.

Duan, P., C. Hu, C. Quan, X. Yi, W. Zhou, M. Yuan, T. Yu, A. Kourouma and K. Yang, 2015. Body mass index and risk of lung cancer: Systematic review and dose-response meta-analysis. Sci. Rep., 19, 16938.

Hidayat, K., X. Du, G. Chen, M. Shi and B. Shi, 2016. Abdominal obesity and lung cancer risk: systematic review and meta-analysis of prospective studies. Nutrients, 8:810.

Hiernaux, J. and J.M. Tanner, 1969. 'Growth and physical studies', In J.S. Weiner, S.A. Lourie (Eds.), Human Biology: A guide to field methods. London: IBP; Oxford, UK: Blackwell Scientific Publications.

Ibrahim, A., H. Khaled, N. Mikhail, H. Baraka and H. Kamel, 2014. Cancer Incidence in Egypt: Results of the National Population-Based Cancer Registry Program. Journal of Cancer Epidemiology, Article ID 437971, 18 pages http:// dx.doi.org/10.1155/2014/437971.

Janssen, I, S. Heymsfield, D. Allison, D. Kotler and R. Ross, 2002. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. Am. J. Clin. Nutr., 75, 683–688.

Kabat, G., M. Kim, J. Hunt, R. Chlebowski and T. Rohan, 2008. Body mass index and waist circumference in relation to lung cancer risk in the Women's Health Initiative. Am. J. Epidemiol., 168, 158–169.

Lam, T., S. Moore, L. Brinton, L. Smith, A. Hollenbeck, G. Gierach and N. Freedman, 2013. Anthropometric measures and physical activity and the risk of lung cancer in never-smokers: A prospective cohort study. PLoS ONE, 8, e70672.

Leitzmann, M., S. Moore, A. Koster, T. Harris, Y. Park, A. Hollenbeck and A. Schatzkin, 2011. Waist circumference as compared with body-mass index in predicting mortality from specific causes. PLoS ONE, 6, e18582.

Ma, Y., Y. Yang, F. Wang, P. Zhang, C. Shi, Y. Zou and H. Qin, 2013. Obesity and risk of colorectal cancer: A systematic review of prospective studies. PLoS ONE, 8, e53916.

Mac, M., R. Hicks, J. Matthews, A. McKenzie, D. Rischin, E.K. Salminen and D.L Ball, 2003. Positron emission tomography is superior to computed tomography scanning for response-assessment after radical radiotherapy or chemoradiotherapy in patients with non-small-cell lung cancer. J Clin Oncol., 21: 1285-1292.

Marquez-Garban, D., V. Mah, M. Alavi, E. Maresh, H. Chen, L. Bagryanova, S. Horvath, D. Chia, E. Garon and L. Goodglick, et al., 2011. Progesterone and estrogen receptor expression and activity in human non-small cell lung cancer. Steroids, 76, 910–920.

Novello, S., T. Vavala, M.G. Levra, F. Solitro, E. Pelosi, A. Veltri and G.V. Scagliotti, 2013. Early response to chemotherapy in patients with non-small-cell lung cancer assessed by [18F]-fluoro-deoxy-D-glucose positron emission tomography and computed tomography. Clin Lung Cancer, 14: 230-237.

Olson, J., P. Yang, K. Schmitz, R. Vierkant, J. Cerhan and T. Sellers, 2002. Differential association of body mass index and fat distribution with three major histologic types of lung cancer: Evidence from a cohort of older women. Am. J. Epidemiol*., 156*, 606–615.

Ramalingam, S., T. Owonikoko and F. Khuri, 2011. Lung cancer: New biological insights and recent therapeutic advances. CA Cancer J Clin., 61: 91-112.

Rebecca, L. Siegel, D. Kimberly Miller, A Jemal, Cancer Statistics, 2018. CA Cancer J Clin., 68 (1):7–30. doi: 10.3322/caac.21442.

Renehan, A. and I. Soerjomataram, 2016. Obesity as an Avoidable Cause of Cancer (Attributable Risks), Obesity and Cancer book, Recent Results in Cancer Research. © Springer International Publishing Switzerland, (243-256), DOI 10.1007/978-3-319-42542-9_13.

Renehan, A., M. Tyson, M. Egger, R. Heller and M. Zwahlen, 2018. Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. Lancet 371, 569–578

Sheikhbahaei, S., E. Mena, A. Yanamadala, S. Reddy, L. Solnes, J. Wachsmann, R. Subramaniam, 2017. The Value of FDG PET/CT in Treatment Response Assessment, Follow-Up, and Surveillance of Lung Cancer, AJR, 208:420–433.

Spiro, S. and G. Silvestri, 2005. One hundred years of lung cancer. Am J Respir Crit Care Med, 172: 523-529.

World Health Organization World Health Organization, 2016, Obesity and overweight, Fact sheet no. 311, Updated January 2015. http://www.who.int/mediacentre/factsheets/fs311/en/.

Yang, Y., J. Dong, K. Sun L. Zhao, F. Zhao, L. Wang and Y. Jiao, 2013. Obesity and incidence of lung cancer: A meta-analysis. Int. J. Cancer, 132, 1162–1169.

Zhao, X., Y. Zhang and Y. Yu, 2018. Use of 18F-FDG PET/CT to predict short-term outcomes early in the course of chemo-radiotherapy in stage III adenocarcinoma of the lung, Oncology Letters 16: 1067-1072,DOI: 10.3892/ol.2018.8748.