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Lipid Status During Combined Treatment in Prostate Cancer Patients

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Abstract

The aim of this study was to provide a specific review of current medical literature regarding the lipid profile during prostate carcinoma (PCa) treatment. The main aim was to analyze the results presented by different authors and to find a commonality in the changes occurring during the treatment—hormonotherapy. The levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol were measured before and after the follow-up treatment. The manuscripts reviewed came from the period between 2008 and 2016. The size of the studies ranged from 16 participants to 310. The mean age was from 65 to 74 years in all studies. The Q test was used to attain all lipid parameters and to specify heterogeneity ($p < .0001$). After 12 months of androgen deprivation therapy (ADT), the patients had a significantly higher level serum TC and TG.

Keywords

prostate cancer, oncology/cancer, androgen deprivation therapy, cholesterol, low-density lipoprotein, triglycerides

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Prostate carcinoma (PCa) is the main cause of mortality among men and the second most common cause of cancer-related mortality (Grubb & Kibel, 2007). The methods of treating PCa patients differ and depend on the age of the patient and the progress of the disease. Radical treatment methods include surgery, radiotherapy (RT), and combinations of both, sometimes combined with hormonotherapy. The androgen dependence of PCa was first described by Huggins (1941) who proved that castration decreases the growth of PCa. Self-contained hormonotherapy is used as neoadjuvant and adjuvant therapy before and after RT, as palliative treatment or with the biochemical prostate-specific antigen (PSA) recurrence. Androgen deprivation therapy (ADT) is carried out by the administration of luteinizing hormone–releasing hormone (LHRH) agonist or antiandrogens. ADT is the standard palliative treatment for metastatic PCa patients and is used as an adjunct to RT in patients with locally advanced disease and in unfavorable intermediate-risk or high-risk disease cases. This kind of treatment is very often used to alleviate the symptoms or to prolong survival. ADT may also promote the development of some changes in metabolism—side effects such as skeletal complications, metabolic and cardiovascular complications, sexual dysfunctions, hot flashes, and mood disorders (Alibhai, Gogov, & Allibhai, 2006; Green et al., 2004; Shahinian, Kuo, Freeman, & Goodwin, 2006). Cholesterol plays an important role in steroidogenesis in which androgens are produced, which in turn stimulate the proliferation of prostate cancer (PCa) cells (Murai, 2015). There are some epidemiological studies that report a positive correlation between hypercholesterolemia or dyslipidemia and PCa (Ahn et al., 2009;

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Hayashi et al., 2012; Kitahara et al., 2011; Mondul, Clipp, Helzlsouer, & Platz, 2010; Moses et al., 2009; Platz et al., 2009; Van Hemelrijck et al., 2011). One epidemiological meta-analysis showed a negative correlation—higher levels of TC, HDL, or LDL were not associated with the risk of development of PCa (YuPeng et al., 2015). The aim of this study was specifically to review the current clinical study–based medical literature regarding the lipid profile in PCa treatment. The plan was to analyze the results presented by different authors and to identify the commonality between changes occurring during treatment.

Materials and Methods

This is a review of all the studies found on the PubMed platform (www.pubmed.com) as a result of a search done with the use of the following keywords: lipid profile in cancer patients; prostate cancer and lipids change; lipid profile in cancer patients after radiotherapy; and lipid profile in prostate cancer patients after chemotherapy. Fifteen studies were found. In these studies the following lipid parameters were compared: TC, HDL, LDL, and TG before and after hormonal therapy. Because the results of two different studies by the same authors were identical, only one of them was included in the review (Study 8—the same authors presented the same data of lipids for two topics in two different journals). One study was omitted in the analysis due to incomplete data (Study 5 had no standard deviation). Two more studies, 2 and 3, were also incomplete due to the lack of full clinical data; however, they were included in the study. Therefore, 13 studies were left (Hamilton et al., 2011; Henriksson, Angelin, & Berglund, 1992; Morote et al., 2015; Nguyen et al., 2015; Oka et al., 2016; Sağlam, Köse, Kumsar, Budak, & Adsan, 2012; Salvador et al., 2013; Smith et al., 2002; Smith, Lee, & Nathan, 2006; Smith et al., 2008; Torimoto et al., 2011; Yuan et al., 2012; Ziaran, Goncalves, & Breza, 2013). The manuscripts came from the period between 2008 and 2016. There were 12 prospective studies and 1 retrospective study. The size of those studies ranged from 16 participants to 310. The mean age was from 65 to 74 years in all studies. All subjects were clinically diagnosed with PCa and the diagnosis was confirmed by histopathological examination and categorized as an advanced clinical stage. The lipid profiles were measured in the blood and monitored at different stages in different studies. The two common monitoring points for all the studies were before the initiation of ADT and 12 months after the treatment. Clinical characteristics of the studies are presented in Table 1.

Statistical Analysis

To synthesize the relevant results from each study, we used meta-analysis. This is an analytical method where the goal is to aggregate and contrast the findings using statistical functions for calculating various effect size or outcome measures. In the conducted meta-analysis, standardized mean differences (SMDs) were estimated between the studies based on the random effects model. Additionally, the Q test was applied to specify heterogeneity of the data. The computation was performed with the metafor R package (Viechtbauer, 2010). Using meta-analysis, the estimates of the standardized mean differences and heterogeneity of the data are reported in Table 2.

Results

The mean difference between baseline concentrations of plasma lipids and the levels after hormonotherapy in the PCa patients is presented in Figures 1–4. It can be seen in Table 2 that for the TC model, the SMD is −0.81, ranging from −1.39 to −0.24, and the p value = .0056. It means that in all aggregated studies we observe a significant increase of TC concentration after RT compared to that before the treatment. However, the tested Q = 140 and $p < .0001$ provide evidence of a considerable amount of heterogeneity in these findings. For HDL and LDL measures, the obtained p values for SMDs are both $>.05$, which indicates an insignificant difference in the lipid concentrations before and after treatment. Similarly the Q test values in HDL and LDL models testify strong heterogeneity of the data. For the final TG lipid, following the synthesized studies, the model indicates statistically significant increase of TG after 12 months therapy compared to that before hormonotherapy. The conducted meta-analysis is displayed graphically in Figures 1–4. Due to lack of data, some studies were excluded from the meta-analyses (see Materials and Methods section).

Discussion

The patients with PCa underwent different treatment modalities, which might have had an influence on the lipid parameters. After hormonal therapy (LHRH analog + antiandrogen bicalutamide or flutamide = maximal androgen blockade [MAB]), prostate cells are deprived of androgen, which decreases proliferation and progression of prostate cancer cells (Pfitzenmaier & Altwein, 2009). Certain studies point to a continuous ADT treatment in older men as the cause of an increased risk of diabetes and fragility fracture but not acute myocardial infarction or sudden cardiac death (Alibhai et al., 2009). There are studies that stand in opposition to the above and state that LHRH agonists do not seem to increase cardiovascular mortality in men with locally advanced prostate cancer (Efstathiou et al., 2009). In a recent epidemiology study, high TC and high HDL levels were presented to be a positive prognostic factor in increasing the overall survival (OS) and disease-free

Table 1. Clinical Characteristics of the Studies.

Title	Authors	n°	ADT n°	LHRHa n°	Orchiectomy n°	Estrogen n°	LHRHa + AA n°	Orchiectomy + AA n°	Lipid fractions	Median age (years)	RT	Observation (months)
1. Analysis of the Lipid Profile and Atherogenic Risk During Androgen Deprivation Therapy in Prostate Cancer Patients	Salvador et al. (2013)	33	33	11			22		TC, HDL, LDL, TG	73.4		6/12
2. Fasting Blood Glucose and Lipid Profile Alterations Following Twelve-Month Androgen Deprivation Therapy in Men With Prostate Cancer	Sağlam et al. (2012)	44	44				18	26	TC, HDL, LDL, TG	74 ± 7		12
3. Metabolic Syndrome and Androgen Deprivation Therapy in Metabolic Complications of Prostate Cancer Patients	Yuan et al. (2012)	125	125		52		73		HDL, TG	72.2 ± 9.3		12
4. The Effects of Androgen Deprivation Therapy on Lipid Metabolism and Body Composition in Japanese Patients With Prostate Cancer	Torimoto et al. (2011)	39	39	14			25		TC, HDL LDL, TG	74.0 + 1.3		3/6/9/12
5. Effect of Androgen Deprivation Therapy on Arterial Stiffness and Serum Lipid Profile Changes in Patients With Prostate Cancer: A Prospective Study of Initial 6-Month Follow-Up	Oka et al. (2016)	58	58	5			53		TC, HDL, LDL, TG	71.8 ± 7.1	18	6
6. Hormonal Regulation of Serum Lp (a) Levels Opposite Effects After Estrogen Treatment and Orchidectomy in Males With Prostatic Carcinoma	Henriksson et al. (1992)	31	15		16	15			TC, HDL, LDL, TG	74.0 ± 1.3		6
7. Metabolic Changes During Gonadotropin-Releasing Hormone Agonist Therapy for Prostate Cancer	Smith et al. (2008)	26	26				26		TC, HDL, LDL, TG	65 ± 10		12
8. Patients With Prostate Cancer Treated by ADT Have Significantly Higher Fibrinogenemia Than Healthy Control	Ziaran et al. (2013)	97	97				97		TC, HDL, LDL, TG	73.4 ± 6.3		12
9. The Metabolic Syndrome and Its Components in Patients With Prostate Cancer on Androgen Deprivation Therapy	Morote et al. (2015)	310	310				310		TC, HDL, LDL, TG	72.0 ± 5.0	40	6/12
10. Changes in Body Composition During Androgen Deprivation Therapy for Prostate Cancer	Smith et al. (2002)	40	40				40		TC, HDL, LDL, TG	66 ± 2.0		12
11. Insulin Sensitivity During Combined Androgen Blockade for Prostate Cancer	Smith et al. (2006)	25	25				25		TC, HDL, LDL, TG	68 ± 2		3
12. Increase in Visceral and Subcutaneous Abdominal Fat in Men With Prostate Cancer Treated With Androgen Deprivation Therapy	Hamilton et al. (2011)	26	26				26		TC, HDL, LDL, TG	70,6 ± 6,8		12
13. Androgen Deprivation Therapy Reversibly Increases Endothelium-Dependent Vasodilation in Men With Prostate Cancer	Nguyen et al. (2015)	16	16				16		TC, HDL, LDL, TG	66 ± 7		6

Note. AA = antiandrogens; ADT = androgen deprivation therapy; LHRHa = luteinizing hormone–releasing hormone analog; RT = radiotherapy; n^0 = number of patients in studies; 1–13 number of studies.

Table 2. Meta-Analysis of the Aggregated Studies for Calculating Effect Size for Lipids Models Before Hormonotherapy and After 12 Months Therapy (SMD and Q Test).

Model	SMD	CI 95%	*p* value	Q test	*p* value
TC	−0.81	[−1.39, −0.24]	.0056	140	<.0001
HDL	−0.58	[−1.82, 0.65]	.3542	428	<.0001
LDL	1.17	[−1.43, 3.77]	.3784	312	<.0001
TG	−0.96	[−1.44, −0.49]	<.0001	108	<.0001

Note. CI = confidence interval; HDL = high-density lipoprotein; LDL = low-density lipoprotein; SMD = standardized mean differences; TG = triglyceride.

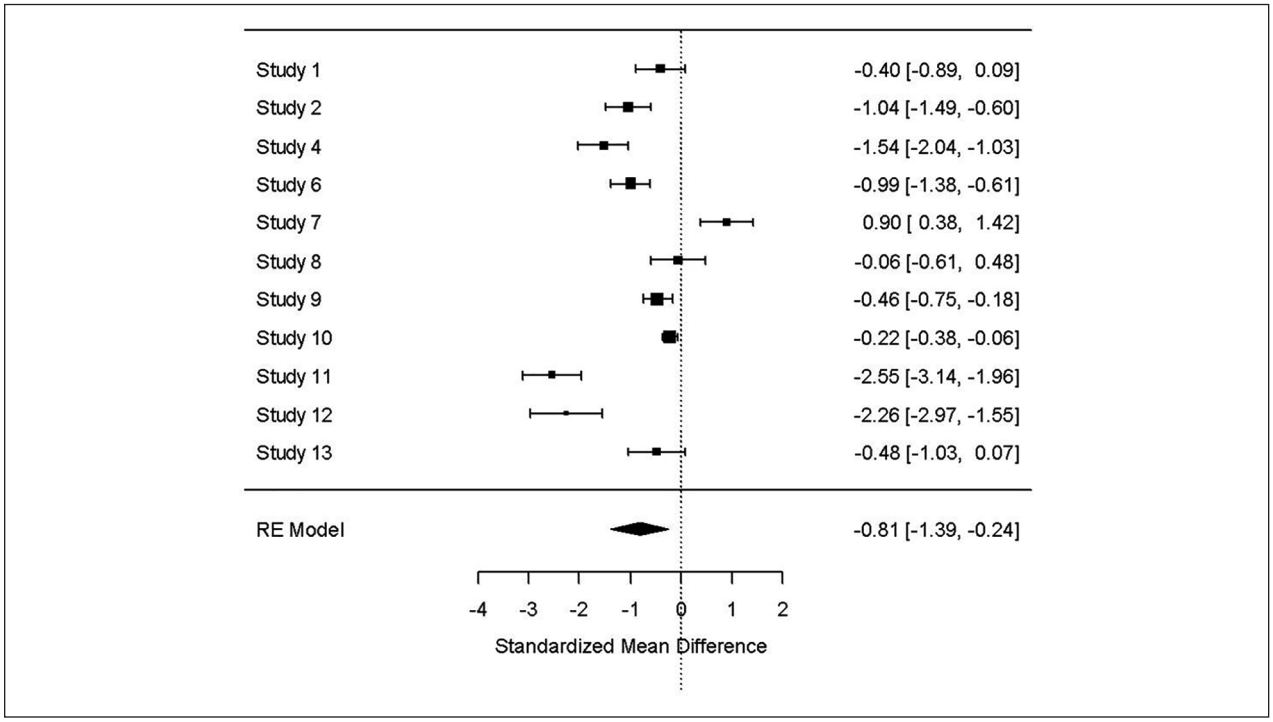

Figure 1. TC: baseline results and 12 months follow-up result for all studies ($p = .0056$).
TC = total cholesterol; RE = random effects.

survival (DFS) among patients with cancer. There was no visible effect of low TG and low LDL on cancer survival. The authors presented certain lipid metabolic markers (high level of TC and LDL and a low level of HDL) as an increased risk factor for the incidence and the progression of cancer (Zhou, Li, Liu, Chen, & Xiao, 2018). TC is an important compound in the human body, especially for transporting proteins in the plasma (Hughes-Fulford, Chen, & Tjandrawinata, 2001) and is used in the synthesis of new cell membranes—including in cancer cells (Banker et al., 2004). Low cholesterol can be a cause of the increased sensitivity to oxidative stress (Muldoon, Kritchevsky, Evans, & Kagan, 1996) and of the loss of immune cells (T cells and CD8+) (Muldoon et al., 1997). In the low serum TC environment, the interleukin-6 level is elevated (an inflammatory protein related with cancer development and progression) (Kuroda et al., 2007). Hypocholesterolemia could occur due to an increased LDL receptor activity in cancer cells (Hughes-Fulford et al., 2001; Vitols, Björkholm, Gahrton, & Peterson, 1985). Long-term use of ADT is known to cause changes in the lipid profile during and after treatment (Alibhai et al., 2009). The results obtained in this analysis reported significantly higher concentrations of total TC and TG after using ADT. The serum lipid levels can be potentially modified by RT: TC was decreased after RT but its reduction was slower in patients with a higher PSA compared to those with a lower PSA and TG decreased after RT only in the patients ≥70 years (Wolny-Rokicka, Tukiendorf, Wydmański, Brzezniakiewicz-Janus, & Zembroń-Łacny, 2019; Wolny-Rokicka, Tukiendorf, Wydmański, & Zembroń-Łacny, 2017). This review aimed to assess the lipid profile in PCa

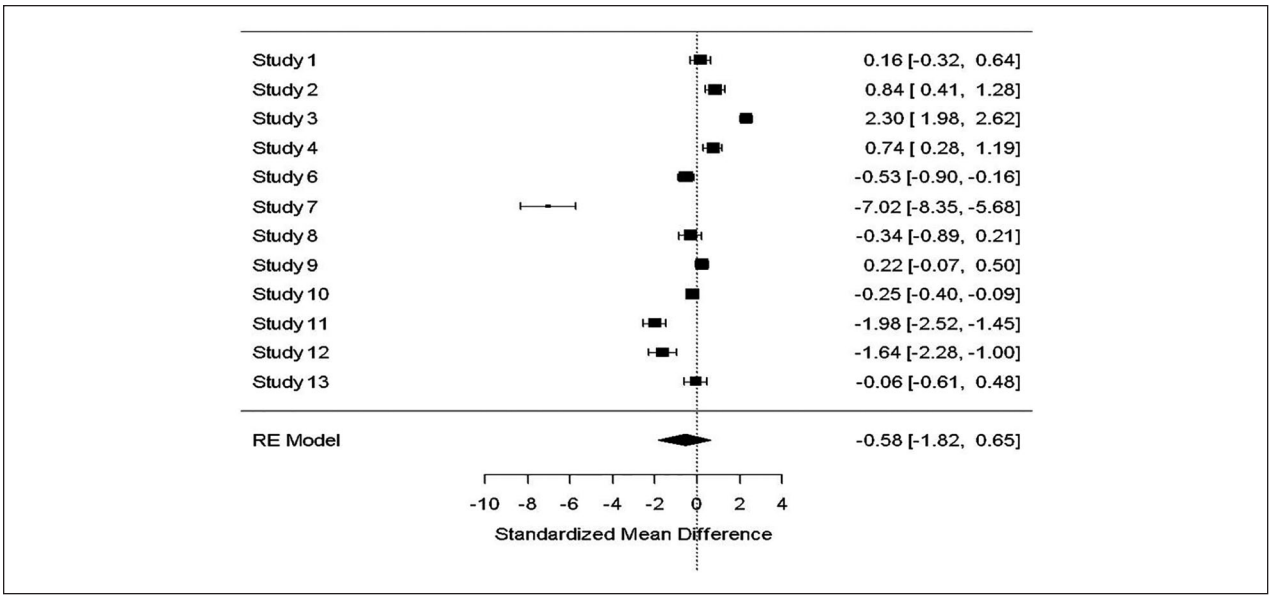

Figure 2. HDL: baseline results and 12 months follow-up result for all studies ($p = .3542$).
HDL = high-density lipoprotein; RE = random effects.

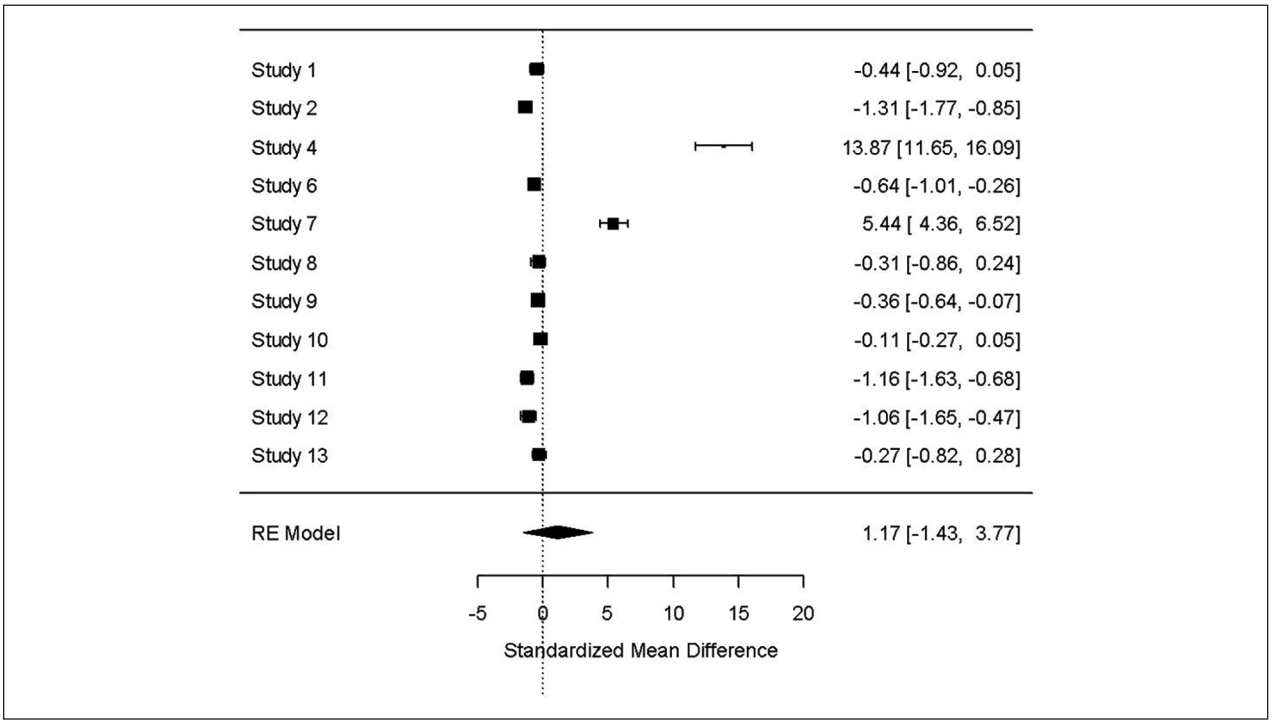

Figure 3. LDL: baseline results and 12 months follow-up result for all studies ($p = .3784$).
LDL = low-density lipoprotein; RE = random effects.

patients during ADT. An overview of medical literature reveals that combining treatment methods works best for PCa patients. Palliative RT when used with ADT contributes to changes in plasma lipids. This is mainly due to changes in the activity of enzymes, their synthesis, and catabolism of lipid membranes, and thus leads to modifications in the composition of lipids (Simons & Sampaio, 2011). PCa cells are reported to have a higher cholesterol and sphingomyelin content when compared with healthy cells (Freeman & Solomon, 2004). The evidence shows

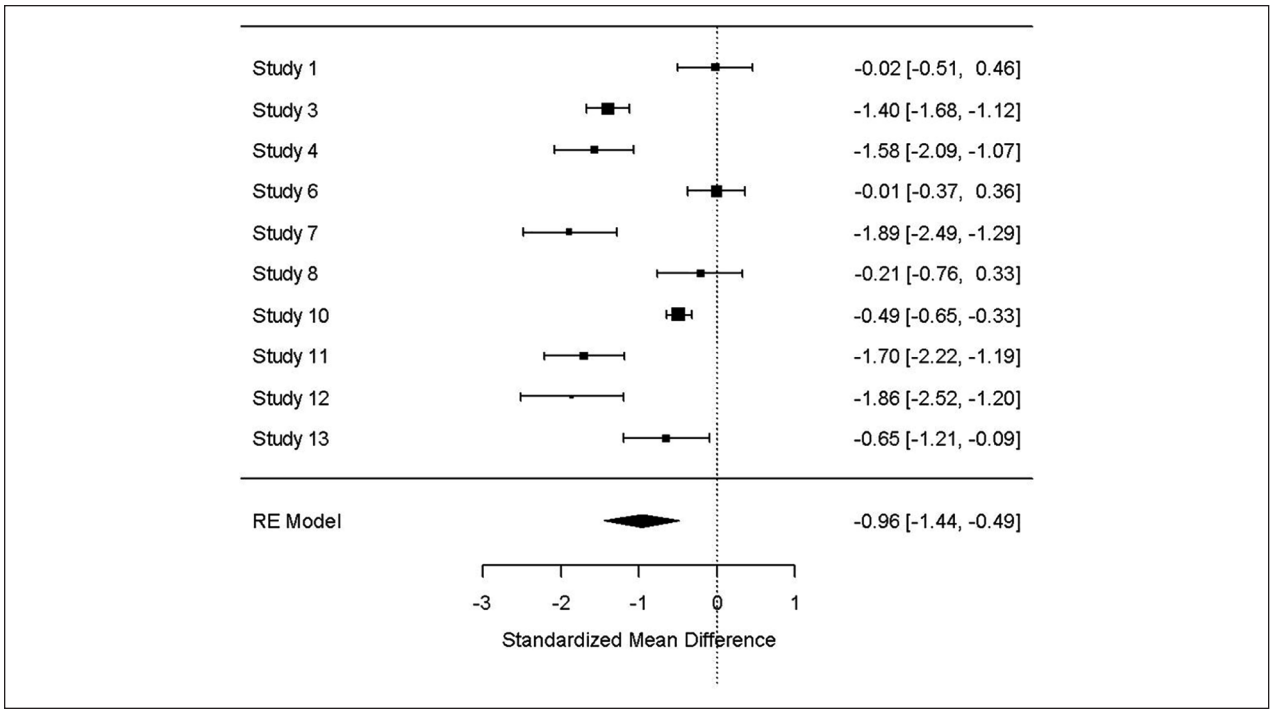

Figure 4. TG: baseline results and 12 months follow-up result for all studies ($p = <.0001$).
TG = triglyceride; RE = random effects.

that PCa cells produce androgen by intratumoral steroidogenesis, leading to their enhanced proliferation (Locke et al., 2008). LDL and HDL stimulate androgen production in steroidogenic tissues (Azhar & Reaven, 2002). In the study on metastatic prostate adenocarcinoma cell lines, LDL induces proliferation of castration-resistant bone-derived cells, but not lymph node metastatic prostate (Sekine et al., 2009). In conclusion, to the best of our knowledge, this is a systematic analysis of the influence of ADT on the lipid profile (TC, TG, HDL, and LDL) in PCa patients. This analysis focused only on examining the correlation between ADT and its effect on the lipid profile in patients. The results showed significantly higher concentrations of total TC and TG after 12 months of the use of ADT. The analysis did not identify any significant differences for HDL and LDL between baseline and after treatment. As the survival rate of cancer patients increases, frequent control of the lipid profile gains importance. In the authors opinion, cholesterol may play multiple roles in promoting PCa. To describe the complete role of lipids in, potential correlation between lipoproteins changes after ADT and progression to castration-resistant prostate cancer should be studied.

Study Limitations

This analysis, however, has certain limitations such as a short follow-up period and the lack of homogeneity in groups and in the methods of treatment. This analysis had different sample sizes of participants involving different populations across the world. In 13 studies, 2 were pooled with RT; hence, hormonotherapy was not the only method of treatment. These studies have no clinical groups of the tumor according to local or advanced stages or clinical tumor, nodes, and metastasis (TNM) stages. Some of the studies had control groups and the time of observations was short—only up to 12 months.

Declaration of Conflicting Interests

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References

Ahn, J., Lim, U., Weinstein, S. J., Schatzkin, A., Hayes, R. B., Virtamo, J., & Albanes, D. (2009). Prediagnostic total and high-density lipoprotein cholesterol and risk of cancer. *Cancer Epidemiology and Prevention Biomarkers*, *18*(11), 2814–2821.

Alibhai, S. M., Duong-Hua, M., Sutradhar, R., Fleshner, N. E., Warde, P., Cheung, A. M., & Paszat, L. F. (2009). Impact of androgen deprivation therapy on cardiovascular disease and diabetes. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, *27*(21), 3452.

Alibhai, S. M., Gogov, S., & Allibhai, Z. (2006). Long-term side effects of androgen deprivation therapy in men with non-metastatic prostate cancer: a systematic literature review. *Critical reviews in oncology/hematology*, *60*(3), 201–215.

Azhar, S., & Reaven, E. (2002). Scavenger receptor class BI and selective cholesteryl ester uptake: partners in the regulation of steroidogenesis. *Molecular and cellular endocrinology*, *195*(1–2), 1–26.

Banker, D. E., Mayer, S. J., Li, H. Y., Willman, C. L., Appelbaum, F. R., & Zager, R. A. (2004). Cholesterol synthesis and import contribute to protective cholesterol increments in acute myeloid leukemia cells. *Blood*, *104*(6), 1816–1824.

Efstathiou, J. A., Bae, K., Shipley, W. U., Hanks, G. E., Pilepich, M. V., Sandler, H. M., & Smith, M. R. (2009). Cardiovascular mortality after androgen deprivation therapy for locally advanced prostate cancer: RTOG 85–31. *Journal of Clinical Oncology*, *27*(1), 92.

Freeman, M. R., & Solomon, K. R. (2004). Cholesterol and prostate cancer. *Journal of cellular biochemistry*, *91*(1), 54–69.

Green, H. J., Pakenham, K. I., Headley, B. C., Yaxley, J., Nicol, D. L., Mactaggart, P. N., . . . Gardiner, R. A. (2004). Quality of life compared during pharmacological treatments and clinical monitoring for non-localized prostate cancer: A randomized controlled trial. *BJU international*, *93*(7), 975–979.

Grubb, R. L., & Kibel, A. S. (2007). Prostate cancer: screening, diagnosis and management in 2007. *Missouri medicine*, *104*(5), 408–13.

Hamilton, E. J., Gianatti, E., Strauss, B. J., Wentworth, J., Lim-Joon, D., Bolton, D., . . . Grossmann, M. (2011). Increase in visceral and subcutaneous abdominal fat in men with prostate cancer treated with androgen deprivation therapy. *Clinical endocrinology*, *74*(3), 377–383.

Hayashi, N., Matsushima, M., Yamamoto, T., Sasaki, H., Takahashi, H., & Egawa, S. (2012). The impact of hypertriglyceridemia on prostate cancer development in patients aged≥ 60 years. *BJU international*, *109*(4), 515–519.

Henriksson, P., Angelin, B., & Berglund, L. (1992). Hormonal regulation of serum Lp (a) levels. Opposite effects after estrogen treatment and orchidectomy in males with prostatic carcinoma. *The Journal of clinical investigation*, *89*(4), 1166–1171.

Hughes-Fulford, M., Chen, Y., & Tjandrawinata, R. R. (2001). Fatty acid regulates gene expression and growth of human prostate cancer PC-3 cells. *Carcinogenesis*, *22*(5), 701–707.

Huggins, C. (1941). Studies on prostatic cancer. II. The effect of castration on clinical patients with carcinoma of the prostate. *Arch. Surg.*, *43*, 209.

Kitahara, C. M., de González, A. B., Freedman, N. D., Huxley, R., Mok, Y., Jee, S. H., & Samet, J. M. (2011). Total cholesterol and cancer risk in a large prospective study in Korea. *Journal of Clinical Oncology*, *29*(12), 1592.

Kuroda, K., Nakashima, J., Kanao, K., Kikuchi, E., Miyajima, A., Horiguchi, Y., . . . Murai, M. (2007). Interleukin 6 is associated with cachexia in patients with prostate cancer. *Urology*, *69*(1), 113–117.

Locke, J. A., Guns, E. S., Lubik, A. A., Adomat, H. H., Hendy, S. C., Wood, C. A., . . . Nelson, C. C. (2008). Androgen levels increase by intratumoral de novo steroidogenesis during progression of castration-resistant prostate cancer. *Cancer research*, *68*(15), 6407–6415.

Mondul, A. M., Clipp, S. L., Helzlsouer, K. J., & Platz, E. A. (2010). Association between plasma total cholesterol concentration and incident prostate cancer in the CLUE II cohort. *Cancer Causes & Control*, *21*(1), 61–68.

Morote, J., Gómez-Caamaño, A., Alvarez-Ossorio, J. L., Pesqueira, D., Tabernero, A., Gómez Veiga, F., . . . Planas, J. (2015). The metabolic syndrome and its components in patients with prostate cancer on androgen deprivation therapy. *The Journal of urology*, *193*(6), 1963–1969.

Moses, K. A., Abd, T. T., Goodman, M., Hsiao, W., Hall, J. A., Marshall, F. F., . . . Issa, M. M. (2009). Increased low density lipoprotein and increased likelihood of positive prostate biopsy in black americans. *The Journal of urology*, *182*(5), 2219–2225.

Muldoon, M. F., Kritchevsky, S. B., Evans, R. W., & Kagan, V. E. (1996). Serum total antioxidant activity in relative hypo-and hypercholesterolemia. *Free radical research*, *25*(3), 239–245.

Muldoon, M. F., Marsland, A., Flory, J. D., Rabin, B. S., Whiteside, T. L., & Manuck, S. B. (1997). Immune system differences in men with hypo-or hypercholesterolemia. *Clinical immunology and immunopathology*, *84*(2), 145–149.

Murai, T. (2015). Cholesterol lowering: Role in cancer prevention and treatment. *Biological Chemistry*, *396* (1), 1–11.396(1), 1–11.

Nguyen, P. L., Jarolim, P., Basaria, S., Zuflacht, J. P., Milian, J., Kadivar, S., . . . Beckman, J. A. (2015). Androgen Deprivation Therapy Reversibly Increases Endothelium-Dependent Vasodilation in Men With Prostate Cancer. *Journal of the American Heart Association*, *4*(4), e001914.

Oka, R., Utsumi, T., Endo, T., Yano, M., Kamijima, S., Kamiya, N., . . . Suzuki, H. (2016). Effect of androgen deprivation therapy on arterial stiffness and serum lipid profile changes in patients with prostate cancer: a prospective study of initial 6-month follow-up. *International journal of clinical oncology*, *21*(2), 389–396.

Pfitzenmaier, J., & Altwein, J. E. (2009). Hormonal therapy in the elderly prostate cancer patient. *Deutsches Ärzteblatt International*, *106*(14), 242.

Platz, E. A., Till, C., Goodman, P. J., Parnes, H. L., Figg, W. D., Albanes, D., . . . Kristal, A. R. (2009). Men with low serum cholesterol have a lower risk of high-grade prostate cancer in the placebo arm of the prostate cancer prevention trial. *Cancer Epidemiology and Prevention Biomarkers*, *18*(11), 2807–2813.

Sağlam, H. S., Köse, O., Kumsar, Ş., Budak, S., & Adsan, Ö. (2012). Fasting blood glucose and lipid profile alterations following twelve-month androgen deprivation therapy in

men with prostate cancer. *The Scientific World Journal, 2012*.

Salvador, C., Planas, J., Agreda, F., Placer, J., Trilla, E., Lopez, M. A., & Morote, J. (2013). Analysis of the lipid profile and atherogenic risk during androgen deprivation therapy in prostate cancer patients. *Urologia internationalis*, *90*(1), 41–44.

Sekine, Y., Koike, H., Nakano, T., Nakajima, K., Takahashi, S., & Suzuki, K. (2009). Remnant lipoproteins induced proliferation of human prostate cancer cell, PC-3 but not LNCaP, via low density lipoprotein receptor. *Cancer epidemiology*, *33*(1), 16–23.

Shahinian, V. B., Kuo, Y. F., Freeman, J. L., & Goodwin, J. S. (2006). Risk of the "androgen deprivation syndrome" in men receiving androgen deprivation for prostate cancer. *Archives of internal medicine*, *166*(4), 465–471.

Smith, M. R., Finkelstein, J. S., McGovern, F. J., Zietman, A. L., Fallon, M. A., Schoenfeld, D. A., & Kantoff, P. W. (2002). Changes in body composition during androgen deprivation therapy for prostate cancer. *The Journal of Clinical Endocrinology & Metabolism*, *87*(2), 599–603.

Smith, M. R., Lee, H., McGovern, F., Fallon, M. A., Goode, M., Zietman, A. L., & Finkelstein, J. S. (2008). Metabolic changes during gonadotropin-releasing hormone agonist therapy for prostate cancer: differences from the classic metabolic syndrome. *Cancer*, *112*(10), 2188–2194.

Smith, M. R., Lee, H., & Nathan, D. M. (2006). Insulin sensitivity during combined androgen blockade for prostate cancer. *The Journal of Clinical Endocrinology & Metabolism*, *91*(4), 1305–1308.

Simons, K., & Sampaio, J. L. (2011). Membrane organization and lipid rafts. *Cold Spring Harbor perspectives in biology*, *3*(10), a004697.

Torimoto, K., Samma, S., Kagebayashi, Y., Chihara, Y., Tanaka, N., Hirayama, A., . . . Hirao, Y. (2011). The effects of androgen deprivation therapy on lipid metabolism and body composition in Japanese patients with prostate cancer. *Japanese journal of clinical oncology*, *41*(4), 577–581.

Van Hemelrijck, M., Garmo, H., Holmberg, L., Walldius, G., Jungner, I., Hammar, N., & Lambe, M. (2011). Prostate cancer risk in the Swedish AMORIS study: the interplay among triglycerides, total cholesterol, and glucose. *Cancer*, *117*(10), 2086–2095.

Viechtbauer, W., (2010). "metafor: Meta-Analysis Package for R. Version 2.1-0", CRAN, https://cran.r-project.org/web/packages/metafor/index.html.

Vitols, S., Björkholm, M., Gahrton, G., & Peterson, C. (1985). Hypocholesterolaemia in malignancy due to elevated low-density-lipoprotein-receptor activity in tumour cells: evidence from studies in patients with leukaemia. *The Lancet*, *326*(8465), 1150–1154.

Wolny-Rokicka, E. I., Tukiendorf, A., Wydmański, J., & Zembroń-Łacny, A. (2017). The comparison and estimation of the prognostic value of lipid profiles in patients with prostate cancer depends on cancer stage advancement. *American journal of men's health*, *11*(6), 1745–1751.

Wolny-Rokicka, E., Tukiendorf, A., Wydmański, J., Brzezniakiewicz-Janus, K., & Zembroń-Łacny, A. (2019). The Effect of Radiotherapy on the Concentration of Plasma Lipids in Elderly Prostate Cancer Patients. *American journal of men's health*, *13*(2), 1557988319846328.

Yuan, J. Q., Tao, X. U., Zhang, X. W., Yu, L. P., Qing, L. I., Liu, S. J., . . . Wang, X. F. (2012). Metabolic syndrome and androgen deprivation therapy in metabolic complications of prostate cancer patients. *Chinese medical journal*, *125*(20), 3725–3729.

YuPeng, L., YuXue, Z., PengFei, L., Cheng, C., YaShuang, Z., DaPeng, L., & Chen, D. (2015). Cholesterol levels in blood and the risk of prostate cancer: a meta-analysis of 14 prospective studies. *Cancer Epidemiology and Prevention Biomarkers*, *24*(7), 1086–1093.

Ziaran, S., Goncalves, F. M., & Sn, J. B. (2013). Complex metabolic and skeletal changes in men taking long-term androgen deprivation therapy. *Clinical genitourinary cancer*, *11*(1), 33–38.

Ziaran, S., Goncalves, F. M., & Breza, J. (2013). Patients with prostate cancer treated by ADT have significantly higher fibrinogenemia than healthy control. *World journal of urology*, *31*(2), 289–292.

Zhou, P., Li, B., Liu, B., Chen, T., & Xiao, J. (2018). Prognostic role of serum total cholesterol and high-density lipoprotein cholesterol in cancer survivors: a systematic review and meta-analysis. *Clinica Chimica Acta*, *477*, 94–104.