ORIGINAL RESEARCH

Effects of Chemotherapy on Serum Lipids in Chinese Postoperative Breast Cancer Patients

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Purpose: Chemotherapy is a comprehensive therapy for breast cancer; nevertheless, its associated adverse effects are drawing increasing attention with the continuous improvement of the efficacy. The changes in serum lipids of breast cancer patients caused by chemotherapy have been reported by previous studies, whereby the former increase the incidence rate of cardiovascular disorders. However, the variations in the changes of serum lipids with different chemotherapy regimens have seldom been reported.

Methods: From January 2011 to December 2017, 1740 breast cancer patients treated with chemotherapy were recruited at the First Affiliated Hospital of Nanjing Medical University. The chemotherapy regimens included anthracycline-based, taxane-based, and anthracycline-plus-taxane-based regimens, dose-dense and standard-interval regimens. Lipid profiles that contained TG (triglyceride), TC (total cholesterol), HDL-C (high-density lipoprotein cholesterol), LDL-C (low-density lipoprotein cholesterol) and Lpa (lipoprotein a) levels were collected prior to the first, second and last cycles of chemotherapy. The changes of serum lipids with the same or different chemotherapy regimens were analyzed and compared.

Results: It was observed that the levels of TG, TC, LDL-C and Lpa increased significantly while that of HDL-C decreased after adjuvant chemotherapy in breast cancer patients (P<0.05). Besides, dose-dense regimens had more influence in TG and HDL-C and less influence in TC and LDL-C than standard-interval regimens. HDL-C was more sensitive to anthracycline-based regimens than taxane-based regimens. The level of TG with anthracycline-plus-taxane-based regimens was higher than that with only anthracycline-based or taxane-based regimens, and the level of HDL-C with anthracycline-plus-taxane-based regimen showed lower than that with taxane-based regimen.

Conclusion: In summary, this study proposed that dyslipidemia was strongly associated with chemotherapy in Chinese breast cancer patients after operative treatment. Furthermore, the changes in levels of serum lipids varied among patients with different chemotherapy regimens and taxane had less effect on dyslipidemia than anthracycline.

Keywords: breast cancer, serum lipids, dyslipidemia, chemotherapy, treatment

Introduction

Breast cancer is the most generally diagnosed cancer and also the most common cause of cancer-related deaths in women globally.[1–3] The mortality rate of breast cancer has decreased dramatically due to the improvements in screening and adjuvant therapies.[4] Numerous treatments are channeled into improving both disease-free survival (DFS) and overall survival (OS) in breast cancer patients, among which adjuvant chemotherapy plays an important role.[5,6] With the great progress made in the positive effects of chemotherapy, the side effects gradually receive increasing attention, which may also affect the survival and prognosis of breast cancer patients.[7]

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The common side effects of breast cancer chemotherapy include bone marrow suppression, anaphylaxis and gastrointestinal reactions, etc. Meanwhile, cardiac toxicity has also been a long-term problem for patients.[8] Many studies have indicated that the levels of blood lipid and lipoprotein in breast cancer patients changed during chemotherapy.[9,10] The unbalanced distribution of lipid and lipoprotein has been proved to be the established risk factor for cardiovascular diseases.[11,12] Therefore, chemotherapy can promote the occurrence and development of cardiovascular diseases in breast cancer patients by inducing dyslipidemia.

Patients with breast cancer receiving adjuvant chemotherapy had a crucial correlation with cardiovascular disease because dyslipidemia is accompanied by high total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), lipoprotein a (Lpa) and low high-density lipoprotein cholesterol (HDL-C). Xin et al analyzed the serum lipid levels of 394 breast cancer patients before and after receiving adjuvant chemotherapy, and observed that TC, TG and LDL-C levels of patients after chemotherapy showed significantly higher than those before chemotherapy, and HDL-C levels were significantly lower.[13] In addition, Grazia et al reported that chemotherapy increased the risk of dyslipidemia in premenopausal and postmenopausal breast cancer patients.[14]

Several studies had revealed that dyslipidemia could be caused by chemotherapy and increased the risks of breast cancer death, recurrence and metastasis.[15,16] Thus, understanding the potentially detrimental effects of chemotherapy on serum lipid levels is critical to enhance the life quality of breast cancer patients in the future, including the improvement of survival, prognosis and reduction of the incidence of complications. However, few studies have been proceeded on the differences in the changes of serum lipids with different chemotherapy regimens in breast cancer patients.[17]

Therefore, the aim of our study is to investigate the association between serum lipids and chemotherapy in Chinese breast cancer patients, and explore the variations of the changes in different chemotherapy regimens.

Methods
Patients
From January 2011 to December 2017, 1740 patients diagnosed with breast cancer were recruited at the First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China, which were selected based on the following eligibility criteria: (1) diagnosed as breast cancer by histopathological examination; (2) stage I–III breast cancer; and (3) treated with surgery followed by chemotherapy. The exclusion criteria were listed for: (1) lack of laboratory data; (2) receiving neo-adjuvant therapy; (3) abnormal cardiopulmonary, liver or kidney function; (4) preexisting primary tumors; (5) patients with related diseases affecting serum lipids; (6) taking related drugs that affect serum lipids; (7) male breast cancer patients. All patients provided informed consent for their clinical data to be reviewed by us. This study was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University and the Helsinki Declaration.

Evaluate Parameters
This study compares the status of lipids and apolipoproteins in 1740 breast cancer patients at different stages in the chemotherapy process. The laboratory parameters relevant to dyslipidemia TC, TG, HDL-C, LDL-C, and Lpa were recorded before chemotherapy, after the first cycle (equal to before the second cycle) and before the last cycle of chemotherapy. The result report was provided by hematology analyzer Sysmex - 800i (Sysmex Corporation, Kobe, Japan). Dyslipidemia was taken into consideration when one of the followings was observed: TC $\geq$ 5.2 mmol/L, TG $\geq$ 1.7 mmol/L, LDL-C $\geq$ 3.4 mmol/L, HDL-C < 1 mmol/L or non-HDL-C $\geq$ 4.1 mmol/L according to Guidelines for Prevention and Treatment of Dyslipidemia in Chinese Adults in 2016. This nonrandomized study also collected other clinical information including age, menopausal status, tumor size, nodal stage, histological grade, hormone receptor status, human epidermal growth factor receptor 2 (HER2), Ki67, molecular subtype and weight. The clinical staging adopted TNM (Tumor Node Metastasis) staging of malignant tumors released by the United States Joint Cancer Committee. Pathological information, including estrogen receptor (ER), progesterone receptor (PR), Her-2, and Ki67, were obtained through immunohistochemical (IHC) analysis. Molecular typing was confirmed by the National Comprehensive Cancer Network (NCCN) guidelines.

Treatment
Adjuvant chemotherapy regimens and dose were determined in accordance with guidelines of the Chinese Society of Clinical Oncology (CSCO) breast cancer, which included: (1) Epirubicin plus Cyclophosphamide (E: 90 mg/m2, C: 600 mg/m2) every 3 weeks for four cycles; (2) Docetaxel

plus Cyclophosphamide (T: 75 mg/m2, C: 600 mg/m2) every 3 weeks for four or six cycles; (3) Epirubicin plus Cyclophosphamide (E: 90 mg/m2, C: 600 mg/m2), followed by paclitaxel (P: 175 mg/m2) every 2 weeks for four cycles; (4) Epirubicin plus Cyclophosphamide (E: 90 mg/m2, C: 600 mg/m2), followed by docetaxel (D: 80 mg/m2) every 3 weeks for four cycles; (5) Docetaxel plus Epirubicin and Cyclophosphamide (T: 75 mg/m2, E: 90 mg/m2, C: 500 mg/m2) every 3 weeks for six cycles. Additionally, there were some other chemotherapy regimens. It was recommended that patients with Her-2 amplification should receive biological targeted therapy with trastuzumab for a full year.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS, Inc, Chicago, IL, USA) software version 22.0 was adopted to analyze the data. Mean and standard deviation (SD) were assessed by performing an independent sample t-test. Chi-square test was conducted to acquire the predictive factors for dyslipidemia from the clinicopathological factors in the univariate analysis. Multivariate binary logistic regression was channeled into identifying the factors that were independently related to dyslipidemia. Median and comparison of levels of serum lipids and apolipoproteins during the same chemotherapy regimens were determined by using random-effects GLS regression. Two-sample Wilcoxon rank-sum (Mann–Whitney) test was used to compare the levels of serum lipids and apolipoproteins in dose-dense with standard-interval chemotherapy regimens. The levels of serum lipids and apolipoproteins among anthracycline-based, taxane-based and anthracycline-plus-taxane-based regimens were compared by using Kruskal–Wallis equality-of-populations rank test. $P<0.05$ was considered to be statistically significant.

Results

A total of 1740 patients were diagnosed with breast cancer by histopathological examination, which includes 149 patients with EC regimen, 139 patients with TC regimen, 53 with TEC regimen, 534 patients with EC-D regimen and 385 patients with EC-P regimen, and the rest of the patients receiving other chemotherapy regimens. Additionally, 194 patients were treated with Trastuzumab and 32 patients with Capecitabine. The average age of these patients was 48.12±9.43 years (range, 21–78 years). Nine hundred and sixty-three patients had dyslipidemia before chemotherapy. ER of 67.18% patients and

HER-2 of 26.55% patients were positive. The characteristics of patients are shown in Table 1.

The relationship between clinicopathological factors and dyslipidemia before chemotherapy is indicated in Tables 2 and 3. In the univariate analysis, age ($P<0.05$), menopausal status ($P<0.05$), PR status ($P<0.05$) and weight ($P<0.05$) were significantly correlated with the occurrence of dyslipidemia. When age, menopausal status, PR status and weight were included into the multivariate analysis, it was observed that age was remained as an independent predictor of dyslipidemia with odds ratio (OR) of 1.796 (95% CI:1.402–2.302, $P<0.05$) and 2.976 (95% CI:1.889–4.688, $P<0.05$), along with menopausal status (OR: 2.143, 95% CI:1.636–2.808, $P<0.05$) and weight (OR:1.407, 95% CI:1.140–1.737, $P<0.05$). However, multivariate analysis showed that PR status ($P>0.05$) had no predictive value for dyslipidemia.

The alterations in the levels of serum lipids and apolipoproteins of 1740 patients during chemotherapy are displayed in Figure 1. The levels of TG for the patients receiving chemotherapy gradually increased ($P<0.05$) and HDL-C gradually decreased ($P<0.05$) during the treatment ($P<0.05$). Compared with those before chemotherapy, the levels of TC and LDL-C reduced after the first cycle, but which significantly increased before the last cycle and showed higher ($P<0.05$). No significant difference was observed in Lpa before and after the first cycle of chemotherapy ($P>0.05$), but it did increase before the last cycle ($P<0.05$).

Comparison of the Levels of Serum Lipids in the Same Regimens

Three hundred and eighty-five breast cancer patients accepted the dose-dense chemotherapy regimens (a) with EC-P every 2 weeks and 502 patients received the standard-interval chemotherapy regimens (b) including EC-D every 3 weeks (Figure 2). The TG levels increased ($P<0.05$) while the HDL-C levels decreased ($P<0.05$) during the treatment of these two regimens. In the previous regimen, TC, LDL-C and Lpa reduced after the first cycle but increased before the last cycle of chemotherapy ($P<0.05$); however, no difference was observed between the levels of before chemotherapy and before the last cycle of chemotherapy in LDL-C and Lpa ($P>0.05$). In the latter regimen, TC, LDL-C and Lpa increased before the last cycle in contrast to those before and after the first cycle ($P<0.05$).

Table I Baseline Characteristics of the Study Population

Characteristics	N	%
Age		
≤45	707	40.63
45–60	843	48.45
>60	190	10.92
Menopausal status		
Premenopausal period	1016	58.39
Perimenopausal period	93	5.35
Postmenopausal period	627	36.03
Missing	4	0.23
Tumor size		
T1	750	43.11
T2	798	45.86
T3	47	2.70
Missing	145	8.33
Nodal stage		
N0	949	54.54
N1	429	24.66
N2	177	10.17
N3	109	6.26
Missing	76	4.37
Histological grade		
I	20	1.15
II	649	37.30
III	868	49.88
Missing	203	11.67
ER		
Positive	1169	67.18
Negative	480	27.59
Missing	91	5.23
PR		
Positive	990	56.90
Negative	659	37.87
Missing	91	5.23
HER-2		
Positive	462	26.55
Negative	1153	66.27
Missing	125	7.18
Ki67		
≤14%	284	16.32
>14%	1344	77.24
Missing	112	6.44
Molecular subtype		
Luminal A	160	9.19
Luminal B	1006	57.82
HER-2	181	10.40
Triple negative	266	15.29

(*Continued*)

Table I (Continued).

Characteristics	N	%
Missing	127	7.30
Weight (kg)		
≤60	1015	58.33
>60	709	40.75
Missing	16	0.92

Then, the anthracycline-based chemotherapy regimens (A) containing anthracycline were selected, which involved 683 breast cancer patients who received EC and the first four times of the cycles of EC-D. One hundred and thirty-nine patients received the taxane-based chemotherapy regimens (B) containing taxane, which consisted of TC every 3 weeks for four or six cycles. Seven hundred and eighty-one patients obtained the anthracycline-plus-taxane-based chemotherapy regimens (C) containing anthracycline and taxane, which included EC-D without Trastuzumab or Capecitabine, EC-P without Trastuzumab and TEC (Figure 3). It was found that TG gradually increased and HDL-C decreased during the treatment (P<0.05) of these three regimens. Compared with the values before the first cycle of chemotherapy in A, TC, LDL-C and Lpa levels significantly increased before the last cycle (P<0.05). In B, TC, LDL-C and Lpa increased after the first cycle (P<0.05) but no difference was demonstrated between their respective levels after the first cycle and before the last cycle of chemotherapy (P>0.05). In C, TC, LDL-C and Lpa decreased after the first cycle but increased before the last cycle of chemotherapy (P<0.05); however, no statistical difference was revealed between the levels of Lpa before chemotherapy and before the last cycle of chemotherapy (P>0.05).

Comparison of the Levels of Serum Lipids in Different Regimens

The levels of serum lipids and apolipoproteins of breast cancer patients treated with dose-dense chemotherapy regimens and standard-interval ones were compared (Figure 4). All data showed that there were no statistical differences between the two chemotherapy regimens before chemotherapy. The level of TG with the standard-interval chemotherapy regimens showed higher than the level with the dose-dense ones after the first cycle of chemotherapy (P<0.05), but the status was reversed before

Table 2 Predictive Factors for Dyslipidemia in Univariate Analyses

Variables	Total (N)	Normal Group (N)	Dyslipidemia Group (N)	p[a]
Age				<0.05
≦45	707	425	282	
45–60	843	309	534	
>60	190	43	147	
Menopausal status				<0.05
Premenopausal period	1016	563	453	
Perimenopausal period	93	38	55	
Postmenopausal period	627	175	452	
Missing	4	1	3	
Tumor size				0.056
T1	751	340	411	
T2	798	332	466	
T3	47	27	20	
Missing	144	78	66	
Nodal stage				0.081
N0	949	430	519	
N1	429	169	260	
N2	177	86	91	
N3	109	53	56	
Missing	76	39	37	
Histological grade				0.519
I	20	11	9	
II	650	295	355	
III	867	379	488	
Missing	203	92	111	
ER				0.077
Positive	1169	538	631	
Negative	480	198	282	
Missing	91	41	50	
PR				<0.05
Positive	988	472	516	
Negative	661	264	397	
Missing	91	41	50	
HER-2				0.319
Positive	463	215	248	
Negative	1153	504	649	
Missing	124	58	66	
Ki67				0.482
≦14%	284	132	152	
>14%	1344	594	750	
Missing	112	51	61	
Molecular subtype				0.199
Luminal A	160	77	83	
Luminal B	1006	459	547	

(*Continued*)

Table 2 (Continued).

Variables	Total (N)	Normal Group (N)	Dyslipidemia Group (N)	p[a]
HER-2	181	74	107	
Triple negative	266	106	160	
Missing	127	61	66	
Weight (kg)				<0.05
≦60	1015	496	519	
>60	709	272	437	
Missing	16	9	7	

Note: [a]Calculated by chi-square test as univariate analyses.

Table 3 Predictive Factors for Dyslipidemia in Multivariate Analyses

Variables	Multivariate OR (95% CI)[a]	p[a]
Age		<0.05
≦45		
45–60	1.796 (1.402–2.302)	<0.05
>60	2.976 (1.889–4.688)	<0.05
Menopausal status		<0.05
Premenopausal period		
Perimenopausal period		0.229
Postmenopausal period	2.143 (1.636–2.808)	<0.05
Missing		
PR		0.192
Positive		
Negative		
Missing		
Weight (kg)		<0.05
≦60		
>60	1.407(1.140–1.737)	
Missing		

Note: [a]Calculated by multivariate binary logistic regression analysis.
Abbreviations: OR, odds ratio; CI, confidence interval.

the last cycle (P<0.05). TC, HDL-C and LDL-C with the standard-interval chemotherapy regimens were higher than those with the dose-dense ones after the first and before the last cycles of chemotherapy (P<0.05). No statistical difference in Lpa existed between the two chemotherapy groups (P>0.05).

The levels of serum lipids and apolipoproteins with anthracycline-based regimens (A), taxane-based regimens (B) and anthracycline-plus-taxane-based regimens (C) were compared, whose results are shown in Figure 5. Comparisons of the levels of serum lipids among the three chemotherapy regimens were made, whose adjusted
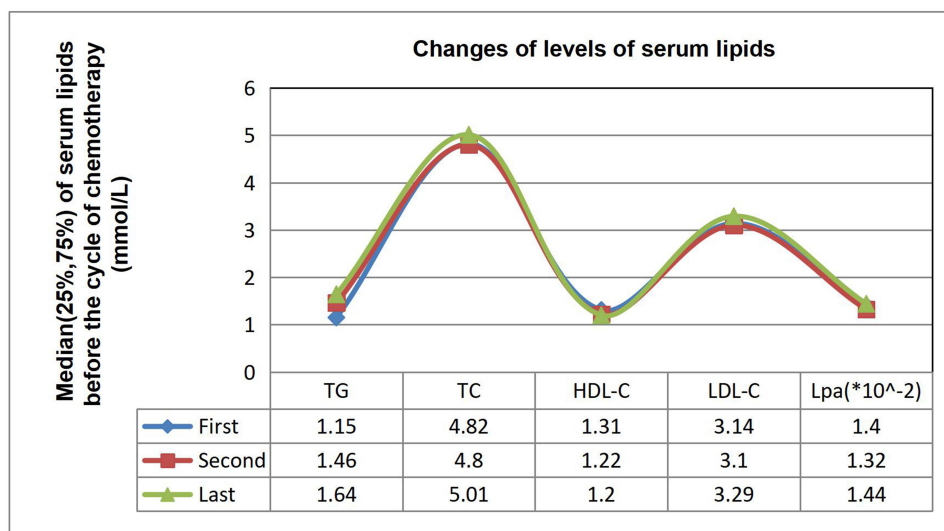
Figure 1 Changes of levels of serum lipids in 1740 patients during chemotherapy. P<0.05 was considered to be statistically significant. All changes were statistically significant except Lpa prior to first and second, second and last cycles of chemotherapy.

p-value for significance was 0.008333. No statistical difference was shown in serum lipids and apolipoproteins among the three chemotherapy regimens before chemotherapy (P>0.05). Comparing the serum lipids of A to B, TG showed higher (P<0.008333), but TC and LDL-C were lower after the first cycle (P<0.008333), and HDL-C was also lower after the first and before the last cycles of chemotherapy (P<0.008333). Comparing the serum lipids of A to C, TG demonstrated lower before the last cycle, but TC and LDL-C were higher after the first cycle of chemotherapy (P<0.008333). Comparing the serum lipids of B to C, TG displayed lower and HDL-C was higher after the first and before the last cycles (P<0.008333), TC and LDL-C were higher after the first cycle of chemotherapy (P<0.008333).

Discussion

The predictive factors of dyslipidemia in breast cancer patients before chemotherapy were founded through univariate and multivariate analysis in the retrospective cohort study. In accordance with previous studies, the age, menopausal status and weight of the patients were closely related to dyslipidemias,[18,19] which suggested that breast cancer patients were more prone to have dyslipidemias with the increases of age and weight.[20] Furthermore, postmenopausal patients had a higher risk of dyslipidemia than premenopausal and perimenopausal patients.[21]

Recently, adjuvant chemotherapy has improved the disease-free survival and overall survival of breast cancer patients; however, the detrimental effects caused by chemotherapy remain unclear.[22–25] We specifically assessed the changes of serum lipids and apolipoproteins following the administration of chemotherapy in breast cancer patients. When the postoperative patients received chemotherapy, their levels of TC and LDL-C reduced after the first cycle because cancer drugs needed cholesterol depletion to cross the cell membranes.[26] However, the TG, TC, LDL-C and Lpa were significantly increased and HDL-C was decreased before the last cycle, which was consistent with previous research results,[27,28] and further confirmed that chemotherapy had adverse effects on postoperative serum lipids of breast cancer patients. The mechanism could be as follows: chemotherapy directly led to endothelial dysfunction and changes in cytokines; chemotherapy caused lipid peroxidation by enhancing systemic oxidative stress to affect the function of liver cells; Meanwhile, chemotherapy affected lipid metabolism by changing the plasma adiponectin level resulting in changes in serum lipid levels.[29–31] Previous studies had revealed that dyslipidemias could also be triggered by endocrine therapy and lipid-lowering therapy was a very successful strategy to prevent cardiovascular events.[32,33] Additionally, dyslipidemias in lung cancer had been proved to increase the activity of tumor cells and reduce their sensitivity to chemotherapy, while its effects on chemotherapy in breast cancer could not be ruled out yet.[34] Thus, it is essential to take certain interventional measures against dyslipidemias in the process of breast cancer treatment.

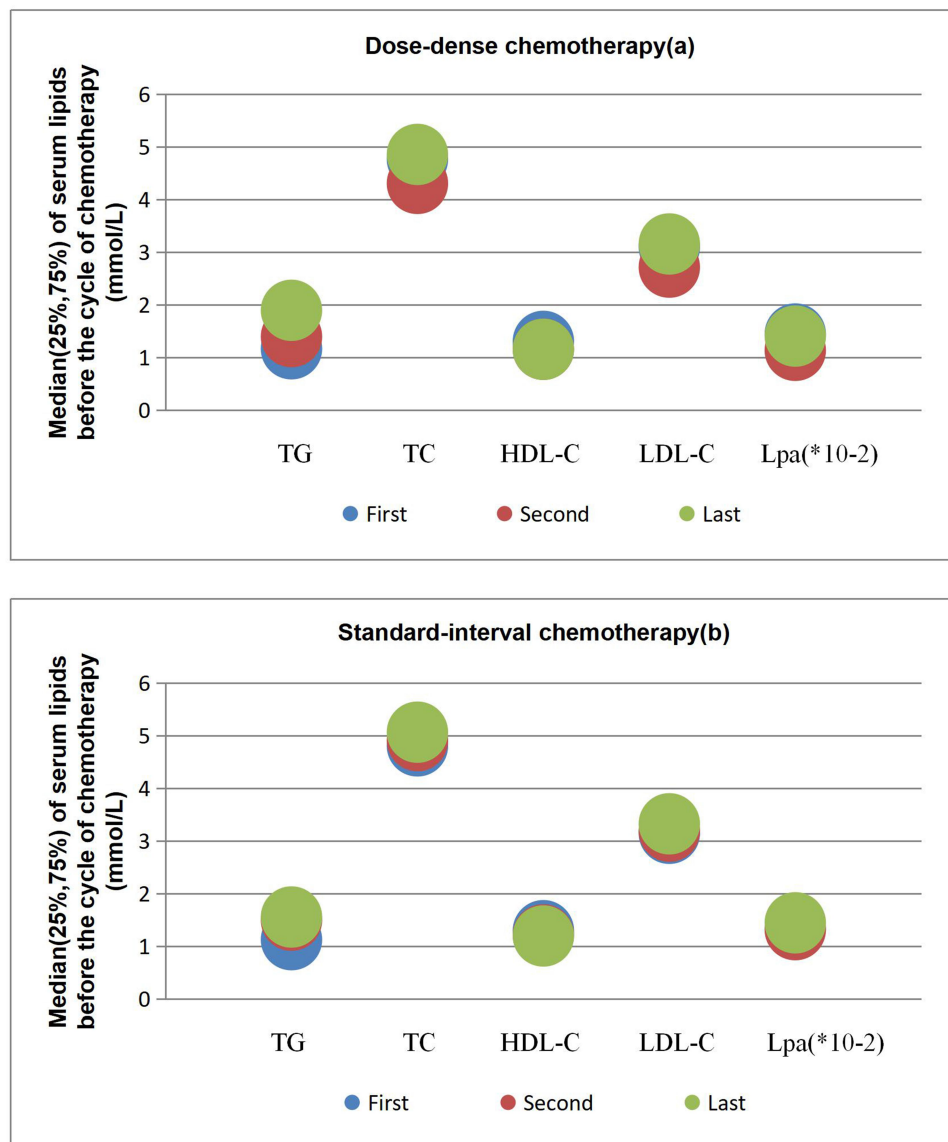**Figure 2** Changes of levels of serum lipids during dose-dense (a) and standard-interval (b) chemotherapy. P<0.05 was considered to be statistically significant. All changes were statistically significant except HDL-C prior to second and last, LDL-C and Lpa prior to first and last cycles in dose-dense chemotherapy and TC, LDL-C and Lpa prior to first and second cycles in standard-interval chemotherapy.

The interval between chemotherapy cycles was regarded as one of the key factors affecting the efficacy of chemotherapy in breast cancer.[35] Many studies reported that the efficacy of dose-dense chemotherapy showed better than that of standard-interval chemotherapy, but few studies compared the differences in their effects on serum lipid levels.[36,37] Previous studies suggested that dose-dense and standard-interval regimens had a similar incidence of myelosuppression,[38] while the results for dyslipidemias were different. After dose-dense chemotherapy, increases in TG and TC, decreases in HDL-C and no significant change in LDL-C and Lpa were observed. TG, TC, LDL-C and Lpa increased but HDL-C reduced after standard-interval

chemotherapy. Due to the same number of chemotherapy cycles, the interval between cycles and the total time of standard-interval regimens were longer than that of dose-dense regimens, and the standard-interval regimens included docetaxel and the dose-dense regimens included paclitaxel. Therefore, the use of docetaxel and the extension of chemotherapy time may cause changes in LDL-C and Lpa. Comparing the two regimens, it was found that TC, HDL-C and LDL-C with standard-interval regimens were higher than those with dose-dense ones. TG with standard-interval regimens was higher than that with dose-dense ones after the first cycle of chemotherapy, but lower before the last cycle of chemotherapy. Obviously, the changes of TC and LDL-C
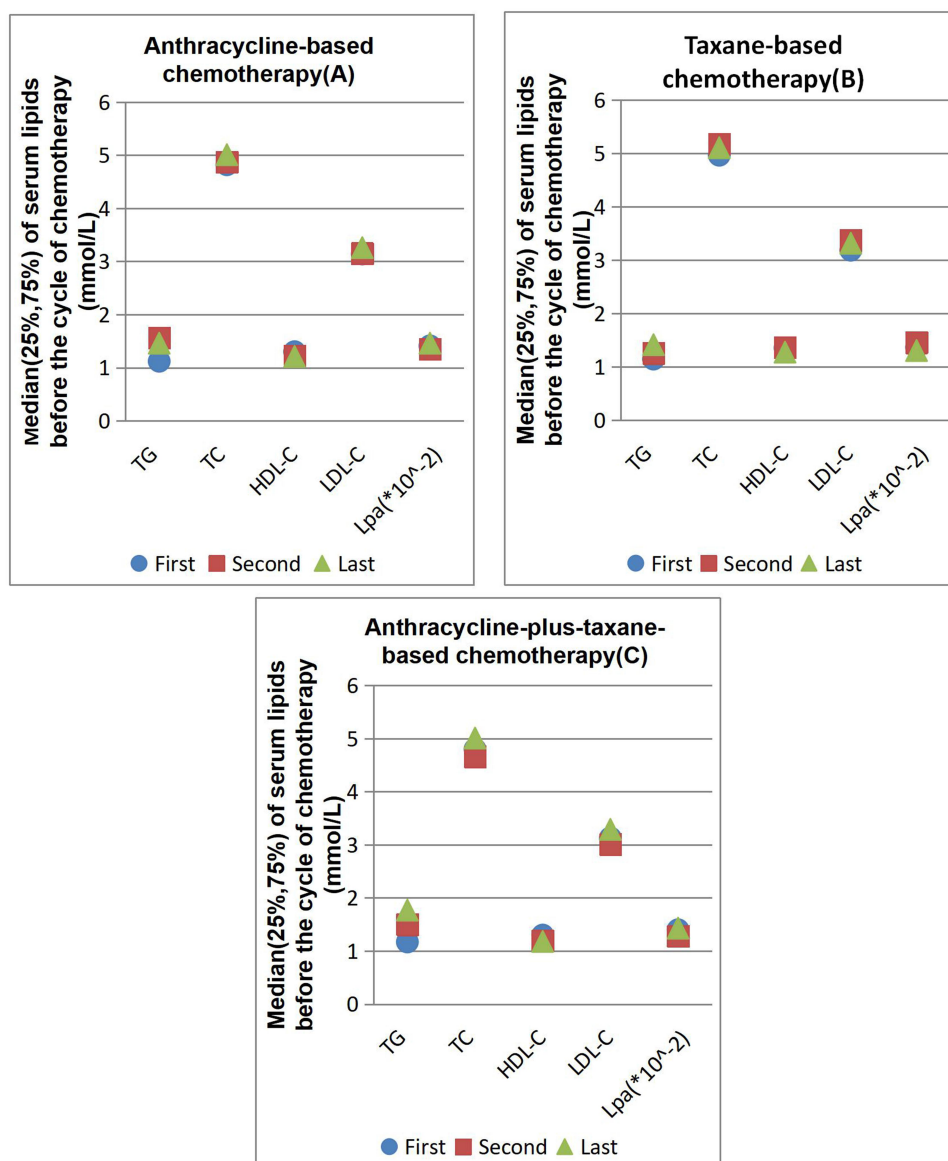
Figure 3 Changes of levels of serum lipids during anthracycline-based (**A**), taxane-based (**B**) and anthracycline-plus-taxane-based (**C**) chemotherapy. All changes were statistically significant except TC, LDL-C and Lpa prior to first and second, Lpa prior to second and last cycles in A, HDL-C prior to first and second, TC, LDL-C and Lpa prior to second and last cycles in B, and Lpa prior to first and last cycles in C.

increased with the extension of the total time of chemotherapy and the use of docetaxel, and the changes of TG and HDL-C increased with the increase of the frequency of chemotherapy and the use of paclitaxel, which was related to the inactivation of cholesterol biosynthesis pathway following paclitaxel treatment.[39] Since there was no difference in drugs, dose and frequency between the two chemotherapy regimens for the first cycle, the difference in serum lipid levels after the first cycle of chemotherapy might be attributed to the deviations from the clinician's chemotherapy regimen based on the clinicopathological information of the patients. Whether there is an increase of TG, TC and LDL-C

or a decrease of HDL-C in elderly, postmenopausal and less tumor-bearing patients after chemotherapy, we need more prospective studies to prove it.

It is well known that anthracycline is the cornerstone of breast cancer chemotherapy; Meanwhile, taxane has been widely adopted in the treatment of breast cancer patients.[40–42] Many clinical trials had found that the taxane incorporated into anthracycline-based chemotherapy regimens could prolong the disease-free survival and overall survival of breast cancer patients.[42–44] This study observed that the levels of TG, TC, LDL-C and Lpa in breast cancer patients increased significantly, while the levels of HDL-C obviously decreased after
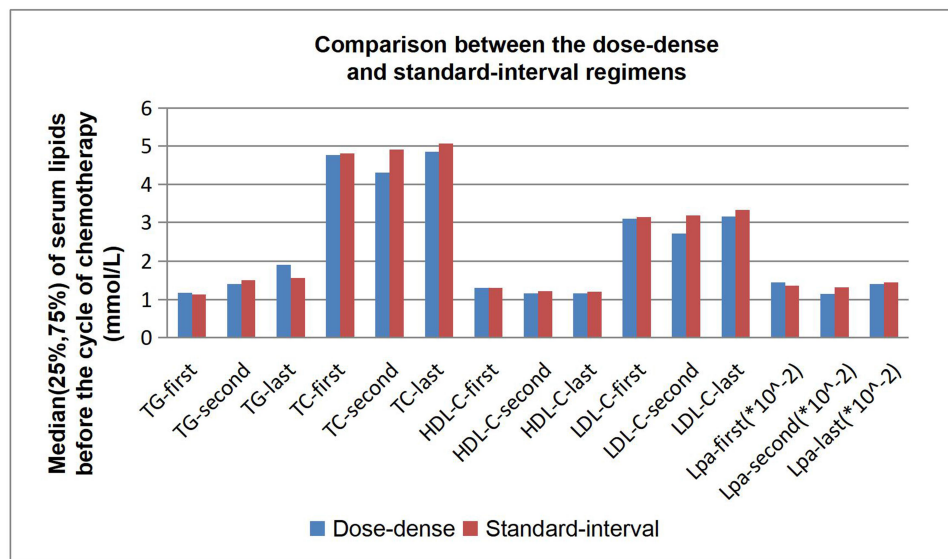
Figure 4 Comparison between the dose-dense and standard-interval regimens. P<0.05 was considered to be statistically significant. There was statistical difference in TG-second, TG-last, TC-second, TC-last, HDL-C-second, HDL-C-last, LDL-C-second and LDL-C-last between dose-dense and standard-interval regimens.
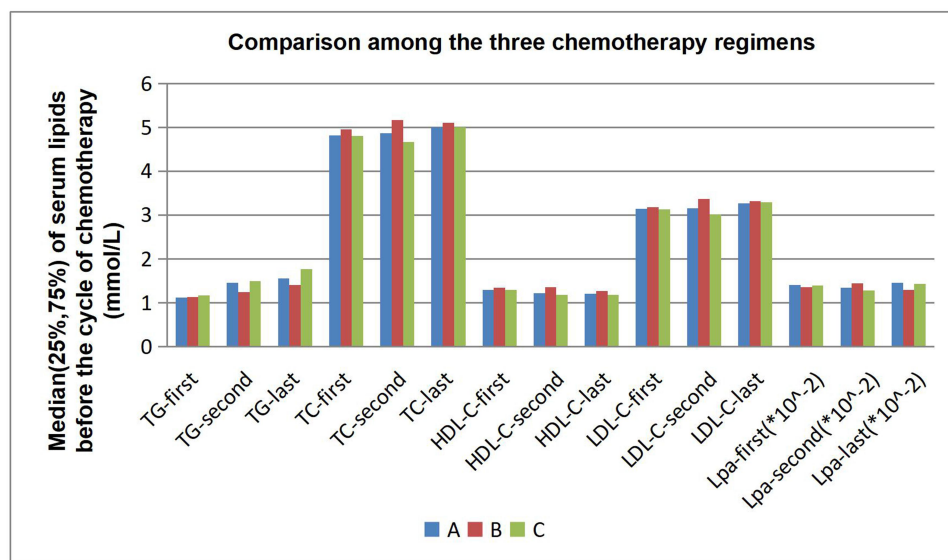

Figure 5 Comparison among anthracycline-based regimens (A), taxane-based regimens (B) and anthracycline-plus-taxane-based regimens (C). The adjusted p-value for significance was 0.008333. There was statistical difference in TG-second, TC-second, HDL-C-second, HDL-C-last and LDL-C-second between A and B, TG-last, TC-second and LDL-C-second between A and C, TG-second, TG-last, TC-second, HDL-C-second, HDL-C-last and LDL-C-second between B and C.

anthracycline-based chemotherapy, which was consistent with previous findings.[45] Some studies proposed that anthracyclines affected hepatocytes metabolism of serum lipids and lipoproteins by reducing the efficiency of mitochondrial respiration and the content of cytoplasmic adenosine triphosphate.[46] Previous studies confirmed taxanes increased the risk of dyslipidemias by inhibiting TC from entering cells, reducing the level of LDL-C receptor protein and promoting the degradation of HDL-C.[47] This study found that TG, TC, LDL-C and

Lpa increased rapidly after patients received the first cycle of taxane-based chemotherapy, while HDL-C as a protective factor for cardiovascular disease did not decrease until the last cycle of chemotherapy. However, studies by Panis et al indicated that the levels of HDL-C, LDL-C and lipoprotein in breast cancer patients injected with short-term single-dose paclitaxel in the first cycle of chemotherapy were significantly lower than those without chemotherapy.[31] It was believed that this variation could be related to the difference in the time of

obtaining blood samples after the first chemotherapy, which was 3 weeks after chemotherapy in this study, whereas it was 3 h after chemotherapy in C. Panis' study. In addition, this study disclosed that the levels of TG, TC and LDL-C increased significantly and HDL-C obviously decreased in breast cancer patients after anthracycline-plus-taxane-based chemotherapy regimens. This result was basically consistent with the results of Bicakli et al, but they found that although the LDL-C of the patients increased, it did not reach the statistical significance.[9] It can be seen that regardless of whether the chemotherapy regimen of breast cancer patients use anthracyclines, taxanes or anthracyclines plus taxanes, abnormalities in serum lipids are almost inevitable. In view of the widespread use of anthracyclines and taxanes in breast cancer chemotherapy, it is conceivable that chemotherapy can lead to dyslipidemias.

In this study, the different effects of anthracycline-based, taxane-based and anthracycline-plus-taxane-based chemotherapy regimens on serum lipids and lipoprotein levels of postoperative breast cancer patients were compared for the first time. In contrast to taxanes, anthracyclines had a greater effect on TG and HDL-C but had a less impact on TC and LDL-C after the first cycle of chemotherapy. Previous studies pointed out that anthracyclines altered TG levels by promoting apoptosis of vascular endothelial cells.[48] Except for HDL-C, the other parameters of the two groups were not statistically significant before the last chemotherapy cycle. Anthracyclines were more likely to cause dyslipidemias than taxanes because of their effect on HDL-C.[47] Compared with anthracycline-plus-taxane-based regimens, TG with anthracycline-based regimens showed lower before the last cycle of chemotherapy, while TC and LDL-C were higher after the first cycle of chemotherapy. Although the short-term effect of anthracyclines plus taxanes on serum lipids was less than that of anthracyclines, the long-term effect was greater than that of anthracyclines, which could be associated with the greater number of chemotherapy cycles. Considering that there was no difference in drugs, dose and frequency between the two first cycles of chemotherapy, it seemed that TC and LDL-C increased more in elderly patients, postmenopausal patients and patients with low tumor load after chemotherapy, which was consistent with our previous speculation. Compared with the anthracycline-plus-taxane-based regimens, patients with taxane-based regimens indicated lower TG levels and higher HDL-C levels after the first cycle and before the last cycle of chemotherapy, but higher TC and LDL-C levels after the first cycle of chemotherapy. Anthracycline plus taxanes had a greater impact on serum lipids than taxanes.[49] It was obvious that anthracyclines plus taxanes were more likely to cause dyslipidemias than anthracyclines, which was more likely to cause dyslipidemias than taxanes. Anthracyclines had a greater effect on TG and HDL-C, while taxanes had a greater effect on TC and LDL-C. Therefore, this result could provide evidence for the selection of lipid-lowering drugs during chemotherapy, and proved that taxanes could be used as the chemotherapy options for patients with high-risk cardiovascular events like hyperlipidemia.

Despite the positive results, the study had some limitations. First of all, as a retrospective study, some relevant influencing factors could not be completely excluded. Secondly, even though the timepoint "after the last chemotherapy" better indicated the effect of chemotherapy on serum lipids, we still selected the timepoint "before the last cycle of chemotherapy" to avoid interference with radiotherapy or endocrine therapy. So our results were still required to be supplemented through rigorous prospective studies. Lastly, our study only evaluated the changes in serum lipids before and during chemotherapy, but lacked the prognostic value of later follow-up. Obviously, the improvement of this part has been carried out.

Conclusion

In conclusion, it was found that chemotherapy resulted in high levels of TG, TC, LDL-C and Lpa and low levels of HDL-C, which could lead to a higher risk of dyslipidemias. Moreover, a significant difference in the changes in levels of serum lipids existed in patients with different chemotherapy regimens. Patients with high TC and LDL-C were more suitable for dose-dense chemotherapy, while patients with high TG and low HDL-C were more suitable for standard-interval one. Furthermore, compared with anthracycline and anthracycline plus taxane regimens, taxane was more suitable for patients with dyslipidemias. As chemotherapy-related side effects are gradually attracting more and more attention, the results can provide guidance for the chemotherapy regimens, as well as the intervention measures and appropriate timing to control the dyslipidemias before and during chemotherapy.

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