RESEARCH ARTICLE

NursingOpen   WILEY

Cardiovascular status of breast cancer patients before and after receiving anthracycline chemotherapy regimen

Zhaoying Dong[1] | Zhaojun Liu[1] | Siyu Chen[1] | Changhong Zhang[2] | Jun Xiao[3] | Xiaoli Zhou[1]

[1]Department of Cardiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

[2]School of Public Health and Management, Research Center for Medicine and Social Development, Collaborative Innovation of Chongqing Medical University, Chongqing, China

[3]Department of Endocrine and Breast Surgery, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

Correspondence
Xiaoli Zhou, Department of Cardiology, The First Affiliated Hospital of Chongqing Medical University, 1 youyi road, Yuzhong district, Chongqing 400000, China.
Email: 2385997378@qq.com

Abstract

Aim: To explore the effect of TEC chemotherapy regimen (Docetaxel + Epirubicin + Cyclophosphamide) on traditional cardiovascular risk factors, atherosclerotic cardiovascular disease and cardiac electrical activity.

Design: 243 patients with first initially diagnosed breast cancer were collected who receiving TEC chemotherapy.

Methods: Univariate analysis, multivariate analysis, binary logistic regression analysis and statistical description were used to analyse the data.

Results: Among the first diagnosed patients, prevalence of hypertension and overweight/obesity in postmenopausal patients were significantly higher than premenopausal group. Compared with initially diagnosed state, incidence of hyperlipidaemia increased significantly after TEC chemotherapy, blood glucose level was remarkably increased, and prevalence of hyperuricaemia was significantly increased, changes of blood pressure level and prevalence rate of hypertension were not significant, and there was no statistical difference. Different menopause status showed the same trend. Atherosclerotic cardiovascular disease risk stratification showed after chemotherapy low-risk patients decrease, medium-risk and high-risk people increased. Grouped by menstrual status, after chemotherapy, both groups showed the same trend. The independent influencing factors of increased heart rate after chemotherapy were postmenopausal status. Postmenopausal patients had more cardiovascular risk factors than premenopausal patients. After receiving chemotherapy, levels of cardiovascular risk factors in both groups mostly changed to the direction of disease. Chemotherapy drugs increase the risk of atherosclerotic cardiovascular disease in breast cancer patients. It is necessary to strengthen interdisciplinary cooperation to dynamic assess the cardiovascular health of patients of breast cancer patients.

KEYWORDS
breast neoplasms, cardiovascular protection, drug therapy, hyperlipidaemias, hyperuricaemia

1 | INTRODUCTION

Breast cancer is the most common malignant tumour among women worldwide. With the progress of diagnosis and treatment, more and more breast cancer patients are able to survive long term. Recently, it has been reported that cardiovascular disease has become the leading cause of death in patients with breast cancer (Patnaik et al., 2011).

Chemotherapy can effectively reduce the risk of recurrence and metastasis of breast cancer. TEC regimen (Docetaxel + Epirubicin + Cyclophosphamide) was recommended by the National Committee on Computer Network guidelines, and its efficacy was widely recognized (Bevers et al., 2018). However, the drug toxicity caused by this regimen was much higher than other regimens. The drug can directly affect the cardiovascular system by the production of reactive oxygen species (McGowan et al., 2017) or indirectly affect the prognosis by cardiovascular problems such as abnormal lipid metabolism. Breast cancer patients with cardiovascular risk factors are more prone to develop drug-related cardiovascular problems after chemotherapy with anthracyclines (Harake et al., 2012). Therefore, it is necessary to understand the cardiovascular status of patients before and after chemotherapy. Although the effect of chemotherapy drugs on cardiovascular health has been recognized clinically, there were few studies on the overall cardiovascular status assessment and risk prediction of patients receiving TEC regimen, and the trend of its change was not entirely clear.

Therefore, the purpose of our study is to observe the routine clinical data of breast cancer patients before and after received TEC chemotherapy, to understand the initial state of cardiovascular risk factors and their evolution after chemotherapy, so as to propose whole-course cardiovascular protection for breast cancer patients.

2 | METHODS

2.1 | Study population and data collection

A total of 243 patients, with an average age of 50.88 ± 9.32 years, who were first diagnosed with primary breast cancer and received TEC chemotherapy were successively collected in the First Affiliated Hospital of Chongqing Medical University, Chongqing Breast Cancer Center, from January 2019 to January 2020. TEC chemotherapy included Epirubicin (75 mg/m^2), Cyclophosphamide (500 mg/m^2) and Docetaxel (75 mg/m^2). There were six courses of treatment, each of which lasted for three weeks.

The following exclusion criteria were applied: (a) a history of malignant cancer; (b) a history of chemotherapy or radiation; (c) non-essential hypertension; (d) male patients; (e) distant metastases of breast cancer; (f) patient history of severe hepatic and renal dysfunction; (g) abnormal thyroid function; (h) patients who received anti-hypertensive, lipid-lowering, hypoglycaemic and uric acid-lowering drugs before the first diagnosis of breast cancer until the end of chemotherapy; and (i) abnormal heart rate requiring clinical intervention

when diagnosis. The following clinical data were collected: baseline data for the first admission of breast cancer and blood pressure, blood lipids, blood glucose, renal function and electrocardiogram. This study was a retrospective survey, and the patient's data were anonymous. The informed consent and ethical approval were not required.

2.2 | Chemotherapy regimen

All enrolled patients received 6 cycles of TEC chemotherapy, with an average cumulative dose of 333.71 mg of anthracyclines. There was no significant difference in the cumulative dose of anthracycline between premenopausal and postmenopausal patients ($p > .05$). It has been previously reported that the cumulative dose of anthracycline was calculated as the result of Epirubicin cumulative dose *0.6(Herait et al., 1992; Nakamae et al., 2004). Each chemotherapy cycle lasted three days. From the first day, take Dexamethasone 10 mg twice a day for three consecutive days; on the second day, intravenous drip of 75 mg/m2 Epirubicin and 500 mg Cyclophosphamide; on the third day, patients received infusion of 75 mg/m2 Docetaxel. Chemotherapy plan took 21 days as one cycle.

2.3 | Laboratory examination

Total cholesterol (TC), total triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein A1(ApoA1), apolipoprotein B (ApoB), lipoprotein α (LPα), fasting blood glucose (FBG), urea, creatinine and uric acid, all results were got from the First Affiliated Hospital of Chongqing Medical University medical examination centre. The medical examination centre was accredited by ISO15189 and certified by CAP.

2.4 | Diagnostic criteria

The diagnosis was based on following criteria: (a) the diagnostic criteria for hypertension in the 2018 European Society of Cardiology and the European Society of Hypertension (ESC/ESH) guidelines (Williams et al., 2018) (blood pressure ≥140/90 mmHg in the consultation room (blood pressure in the consultation room is measured repeatedly) or daytime blood pressure outside of the clinic ≥135/85 mmHg and nocturnal blood pressure outside of the clinic ≥120/70 mmHg); (b) the "Guidelines for the prevention and treatment of dyslipidaemia in Chinese adults (2016 revised edition)" (Chu Junren et al., 2016) (at least one of the following: TC ≥ 6.2 mmol/L, TG ≥ 2.3 mmol/L, HDL-C < 1 mmol/L and LDL-C ≥ 4.1 mmol/L); (c) the 1999 World Health Organization/International Diabetes Federation diagnostic criteria for diabetes(Glucose tolerance and mortality, 1999) (including FBG ≥7.0 mmol/L, random glucose ≥11.1 mmol/L, or 2 hr oral glucose tolerance test (OGTT) ≥11.1 mmol/L);(d) the "Chinese multi-disciplinary consensus on

the diagnosis and treatment of hyperuricaemia and its related diseases" (Multi-Disciplinary Expert Task Force on Hyperuricemia and Its Related Diseases, 2017) (Fasting blood UA levels were observed twice on different days on a normal purine diet, for female >420 umol/L (7.06 mg/dl)); (e)"The guidelines for the prevention and control of overweight and obesity in Chinese adults (2003)" (Chen et al., 2004) (in Chinese adults, the cut-off for overweight is a body mass index (BMI) of 24 kg/m2, while the cut-off for obesity is a BMI of 28 kg/m2); (f) the "Chinese Guidelines for Menopausal Management and Hormone Therapy (2018)" (Qi, 2018) (if 12 months after the last menstrual period, there was still no menstrual period, the patient could be clinically diagnosed with menopause after the exclusion of the possibility of pregnancy); (g)the "Guidelines for the prevention and treatment of dyslipidemia in Chinese adults (2016 Revision)" (patients with a history of ASCVD were considered to be at extremely high risk, an ASCVD risk ≥10% was considered a high level of risk, an ASCVD risk from 5%–9% was considered a moderate level of risk, and an ASCVD risk <5% was considered a low level of risk) (Chu Junren et al., 2016); and (h) The Laboratory Department of the First Affiliated Hospital of Chongqing Medical University is a medical laboratory accredited by ISO15189 and certified by CAP.

2.5 | Blood pressure test

Within 2 days of admission, blood pressure was measured at different time points in resting state, twice each time and take averaged.

2.6 | ECG examination

The ECG was recorded by "MEDED" mobile wireless network system. ECG was measured at 25 mm/s speed and all data of statistical analysis were calculated and reported automatically. All data were automatically calculated, and reports were written by the same ECG specialist and reviewed by another ECG specialist.

2.7 | Statistical analysis

SPSS 26.0 statistical software was used for analysis. The categorical variables were described by frequency and compared by chi-square test. Means ± standard deviation (mean ± *SD*) was used to describe the continuous variables both satisfying the normal distribution and homogeneity of variance and compared by use of independent-sample *t* test. Other continuous variables were expressed as median and interquartile range and compared by Mann–Whitney U test. $p < .05$ were regarded statistically different. Binary logistics regression looked for independent influencing factors for occurrence of increased resting heart rate. In this study, backward elimination was used to identify variables that were independent risk factors. $p < .1$ was considered to indicate a significant difference.

3 | RESULTS

3.1 | Basic characteristics of the study population

Among 243 patients in this study, the average age was 51.43 years (27–72 years). 141 (58.02%) lived in cities and 102 (41.98%) lived in rural areas, 136 cases (55.97%) were premenopausal and 107 cases (44.03%) were postmenopausal. 228 (93.83%) had a history of fertility, and 15 (6.17%) had no history of fertility.

3.2 | Baseline combination of cardiovascular risk factors in the study population

Overall combination of cardiovascular risk factors in this group of patients: the whole group of 243 cases, 61 cases of hypertension (25.1%), 76 cases (31.3%) of hyperlipidaemia, 7 cases (2.9%) had type 2 diabetes, 6 cases (2.5%) were found to have hyperuricaemia, 94 cases (47.0%) were overweight and obesity, and 5 cases (2.1%) have been diagnosed as coronary heart disease. The combination of cardiovascular risk factors in premenopausal and postmenopausal breast cancer patients: the prevalence of postmenopausal group complicated with hypertension, hyperlipidaemia and diabetes was statistically significantly different from that in the premenopausal group ($p < .05$) (Table 1).

3.3 | Effects of TEC chemotherapy regimens on cardiovascular risk factors in breast cancer patients

3.3.1 | Blood pressure

After receiving TEC chemotherapy, there was no significant change in blood pressure of breast cancer patients compared with before chemotherapy. The prevalence of hypertension was slightly higher than that before chemotherapy, but there was no statistically significant difference ($p > .05$). Grouped according to menopause or not, there was no significant change in blood pressure level after chemotherapy compared with before; the prevalence of hypertension was higher than that before chemotherapy, but there was no statistically significant difference ($p > .05$) (Table 2).

3.3.2 | Blood lipid

After receiving TEC chemotherapy, the levels of TC, TG, LDL-C and ApoA1 in breast cancer patients increased; while the levels of HDL-C and ApoA1 decreased, there was a statistically significant difference compared with those before chemotherapy ($p < .05$), and the prevalence of hyperlipidaemia was also significantly increased, and the difference was statistically significant ($p < .05$). Grouping by menopausal or not, the levels of TC, TG, LDL-C and ApoB were increased in premenopausal breast cancer patients, while the levels of HDL-C

TABLE 1 Baseline combination of cardiovascular risk factors in the study population (n = 243)

Characteristics	All (n = 243) No.(%)	Premenopausal (n = 132) No.(%)	Postmenopausal (n = 111) No.(%)	χ^2	p
Overweight/Obesity	94 (47.00)	44 (41.12)	50 (53.76)	3.192	0.074
Missing	43 (Of the total)	25 (Of the total)	18 (Of the total)		
Hypertension	61 (25.10)	24 (18.18)	37 (33.33)	7.362	*0.007*
Hyperlipidaemia	76 (31.28)	31 (23.48)	45 (40.54)	8.160	*0.004*
Type 2 diabetes	7 (2.88)	1 (0.76)	6 (5.40)	4.656	*0.031*
Hyperuricaemia	6 (2.47)	3 (2.27)	3 (2.70)	0.046	0.830

Note: Bold values indicate $P < 0.005$.

TABLE 2 Blood pressure of enrolled patients (n = 243)

Demographic characteristics	Baseline condition	Post-treatment condition	U/χ^2 valves	p valves
Overall situation				
Systolic pressure (mmHg)	122 (111, 135)	120 (115, 133)	−0.004	0.997
Diastolic blood pressure (mmHg)	78 (71, 84))	76 (72, 81)	−1.421	0.155
Hypertension, n (%)	61 (25.10)	63 (25.93)	0.043	0.835
Premenopausal group				
Systolic pressure (mmHg)	118 (110, 128)	119 (112, 127)	0.397	0.691
Diastolic blood pressure (mmHg)	77 (71, 83)	76 (70, 80)	−1.545	0.122
Hypertension, n (%)	24 (18.18)	25 (18.94)	0.025	0.874
Postmenopausal group				
Systolic pressure (mmHg)	128 (116, 143)	125 (116, 140)	−0.566	0.572
Diastolic blood pressure (mmHg)	79 (71, 85)	78 (74, 85)	−0.473	0.636
Hypertension, n (%)	37 (33.33)	38 (34.23)	0.020	0.887

and ApoA1 were decreased, showing statistically significant differences compared with those before chemotherapy ($p < .05$). Similarly, the levels of TC, TG, LDL-C and ApoB in postmenopausal breast cancer patients increased, while the levels of HDL-C and ApoA1 decreased, and the levels of TG, HDL-C and ApoA1 ApoB were significantly different from those before chemotherapy ($p < .05$). In addition, compared with before chemotherapy, the prevalence of hyperlipidaemia after chemotherapy was significantly increased in both groups ($p < .05$) (Table 3).

3.3.3 | Blood glucose

After receiving TEC chemotherapy, fasting blood glucose levels in breast cancer patients increased and there were significantly different from those before chemotherapy ($p < .05$); the prevalence of diabetes increased, but there was no statistically significant difference from that before chemotherapy ($p < .05$). Grouped according to whether menopause, fasting blood glucose level in both groups was increased and the difference was significant compared with that before chemotherapy ($p < .05$), but there was no significant increase in the prevalence of diabetes compared with before chemotherapy ($p > .05$) (Table 4).

3.3.4 | Renal function

After receiving TEC chemotherapy, urea and creatinine levels in breast cancer patients decreased significantly. The levels of uric acid increased significantly; the difference was significant compared with that before chemotherapy ($p < .05$). The prevalence of hyperuricaemia was increased, with statistically significant difference ($p < .05$). Grouping analysis according to menopause or not, the levels of creatinine in breast cancer patients in the two groups were significantly different from those before chemotherapy ($p < .05$) The levels of serum uric acid and the prevalence of hyperuricaemia in premenopausal patients increased after chemotherapy, and there were significant differences compared with those before chemotherapy ($p < .05$). The levels of urea and creatinine in menopausal patients were significantly changed before and after chemotherapy ($p < .05$) (Table 5).

3.4 | The effect of TEC chemotherapy regimen on ECG of breast cancer patients

After receiving TEC chemotherapy, breast cancer patients have increased resting heart rate and prolonged QTc interval, and the

TABLE 3 Blood lipid of enrolled patients (*n* = 243)

Demographic characteristics	Baseline condition	Post-treatment condition	U/T/χ² valves	*p* valves
Overall situation				
Total cholesterol (mmol/L)	4.42 (3.87, 4.92)	4,71 (4.15, 5.24)	3.057	*0.002*
Total triglycerides (mmol/L)	1.09 (0.78, 1.44)	1.51 (1.08, 2.11)	6.885	*0.000*
High-density lipoprotein cholesterol (mmol/L)	1.43 (1.19, 1.67)	1.23 (0.99, 1,45)	−6.055	*0.000*
Low-density lipoprotein cholesterol (mmol/L)	2.73 (2.31, 3.25)	2.99 (2.55, 3.53)	3.627	*0.000*
Apolipoprotein A1 (mmol/L)	1.49 (1.31, 1.68)	1.38 (1.21, 1.51)	−5.156	*0.000*
Apolipoprotein B (mmol/L)	0.85 (0.72, 1.02)	0.95 (0.82, 1.11)	4.600	*0.000*
Lipoprotein(a) (mmol/L)	75.00 (36.00, 211.00)	91.00 (42.00, 226.50)	1.138	0.225
Hyperlipidaemia, *n* (%)	76 (31.28)	117 (48.15)	14.447	*0.000*
Premenopausal group				
Total cholesterol (mmol/L)	4.24 (3.79,4.70)	4.62 (4.03, 5.12)	3.565	*0.000*
Total triglycerides (mmol/L)	1.04 (0.71, 1.38)	1.44 (1.08, 2.03)	5.628	*0.000*
High density lipoprotein cholesterol (mmol/L)	1.41 (1.18, 1.64)	1.24 (0.99, 1.50)	−3.579	*0.000*
Low density lipoprotein cholesterol (mmol/L)	2.52 (2.22, 3.16)	2.89 (2.42, 3.45)	3.612	*0.000*
Apolipoprotein A1 (mmol/L)	1.44 (1.27, 1.65)	1.38 (1.17, 1.53)	−2.284	*0.022*
Apolipoprotein B (mmol/L)	0.79 (0.67, 0.94)	0.94 (0.78, 1.04)	4.386	*0.000*
Lipoprotein(a) (mmol/L)	68.00 (34.50, 154.75)	95.00 (39.50, 211.50)	1.207	0.227
Hyperlipidaemia, *n* (%)	31 (23.48)	57 (43.18)	11.523	*0.001*
Postmenopausal group				
Total cholesterol (mmol/L)	4.73 (4.12, 5.31)	4.75 (4.21, 5.29)	0.551	0.582
Total triglycerides (mmol/L)	1.21 (0.85, 1.56)	1.54 (1.08, 2.18)	4.081	*0.000*
High-density lipoprotein cholesterol (mmol/L)	1.46 (1.20, 1.71)	1.18 (1.00, 1.42)	−5.063	*0.000*
Low-density lipoprotein cholesterol (mmol/L)	3.00 (2.50, 3.46)	3.17 (2.69, 3.62)	1.456	0.145
Apolipoprotein A1 (mmol/L)	1.54 (1.36, 1.72)	1.37 (1.22, 1.50)	−5.305	*0.000*
Apolipoprotein B (mmol/L)	0.92 (0.77, 1.07)	0.98 (0.86, 1.17)	2.156	*0.031*
Lipoprotein(a) (mmol/L)	85.00 (44.00, 271.50)	89.00 (47.00, 265.00)	0.362	0.718
Hyperlipidaemia, *n* (%)	45 (40.54)	60 (54.05)	4.066	*0.044*

Note: Bold values indicate *P* < 0.005.

Demographic characteristics	Baseline condition	Post-treatment condition	U/T/χ² valves	*p* valves
Overall situation				
Fasting blood glucose (mmol/L)	5.20 (4.90, 5.60)	5.54 (5.22, 5.94)	6.746	*0.000*
Diabetes, *n* (%)	7 (2.88)	16 (6.58)	3.697	0.055
Premenopausal group				
Fasting blood glucose (mmol/L)	5.05 (4.80, 5.40)	5.33 (5.07, 5.72)	5.125	*0.000*
Diabetes, *n* (%)	1 (0.76)	5 (3.79)	2.729	0.213
Postmenopausal group				
Fasting blood glucose (mmol/L)	5.40 (5.00, 5.80)	5.84 (5.50, 6.30)	4.984	*0.000*
Diabetes, *n* (%)	6 (4.55)	11 (8.33)	1.593	0.207

TABLE 4 Diabetes of enrolled patients (*n* = 243)

Note: Bold values indicate *P* < 0.005.

differences were statistically significant compared with those before chemotherapy (*p* < .05). Grouped by whether menopause, the resting heart rate and the QTc interval prolonged in both groups increased, and the difference was significant compared with that before chemotherapy (*p* < .05) (Table 6).

3.5 | ASCVD risk stratification in breast cancer patients before and after TEC chemotherapy

ASCVD status of first diagnosed breast cancer patients: ASCVD risk stratification in first-diagnosis breast cancer patients: low-risk

TABLE 5 Renal function of enrolled patients (n = 243)

Demographic characteristics	Baseline condition	Post-treatment condition	U/T/χ^2 valves	p valves
Overall situation				
Carbamide (mmol/L)	4.80 (4.00, 5.70)	4.50 (3.70, 5.40)	−2.642	**0.008**
Creatinine (mmol/L)	60.00 (54.00, 65.25)	53.00 (48.00, 58.00)	−8.034	**0.000**
Urea acid (mmol/L)	267.50 (236.00, 312.00)	296.00 (256.50, 335.00)	4.317	**0.000**
Hyperuricaemia, n (%)	6 (2.47)	18 (7.41)	6.312	**0.012**
Premenopausal group				
Carbamide (mmol/L)	4.40 (3.80, 5.20)	4.55 (3.68, 5.33)	−0.396	0.692
Creatinine (mmol/L)	59.00 (53.00, 64.00)	53.00 (47.00, 57.00)	−5.967	**0.000**
Urea acid (mmol/L)	259.00 (228.00, 305.00)	300.00 (256.00, 339.00)	4.148	**0.000**
Hyperuricaemia, n (%)	3 (2.27)	13 (9.85)	6.653	**0.010**
Postmenopausal group				
Carbamide (mmol/L)	5.20 (4.20, 6.20)	4.50 (3.70, 5.70)	−3.461	**0.001**
Creatinine (mmol/L)	61.00 (55.00, 67.00)	54.00 (48.00, 60.00)	−5.488	**0.000**
Urea acid (mmol/L)	282.00 (243.00, 319.00)	290.00 (261.00, 332.00)	0.916	0.134
Hyperuricaemia, n (%)	3 (2.70)	5 (4.50)	0.519	0.471

Note: Bold values indicate $P < 0.005$.

TABLE 6 The effect of TEC chemotherapy regimen on ECG of breast cancer patients (n = 243)

Demographic characteristics	Baseline condition	Post-treatment condition	U/T/χ^2 valves	p valves
Electrocardiogram data				
Heart rate, Mean ± SD	76.20 ± 10.89	80.32 ± 10.76	−4.194	**0.000**
QT, Median (IQR)	374.00 (360.00, 392.00)	372.00 (354.00, 390.00)	−1.755	0.079
QTc interval, Median (IQR)	421 (409, 432)	427 (416, 436)	−3.752	**0.000**
PR interval, Median (IQR)	146 (136, 162)	150 (138, 164)	−1.890	0.059
Idiopathic QRS axis catheter ablation, Mean ± SD	38.71 ± 30.74	36.26 ± 29.46	0.897	0.370
QRS, Median (IQR)	39 (16, 61)	35 (15, 58)	−0.977	0.329
RV5+SV1, Mean ± SD	1.77 ± 0.54	1.72 ± 0.53	1.127	0.260
Premenopausal group				
Heart rate, Mean ± SD	77.41 ± 11.75	80.54 ± 11.62	−2.176	**0.030**
QT, Median (IQR)	370.00 (356.50, 389.50)	372.00 (350.00, 388.00)	−0.614	0.539
QTc interval, Median (IQR)	420.00 (406.00, 432.00)	426.00 (413.00, 435.75)	2.089	**0.037**
PR interval, Median (IQR)	146.00 (136.00, 160.00)	148.00 (138.00, 164.00)	1.473	0.141
Idiopathic QRS axis catheter ablation, Mean ± SD	43.42 ± 31.45	42.35 ± 30.33	0.282	0.778
QRS, Median (IQR)	80.00 (74.00,84.00)	80.00 (72.00, 86.00)	0.120	0.905
RV5+SV1, Mean ± SD	1.73 ± 0.53	1.71 ± 0.53	0.374	0.709
Post-menopausal group				
Heart rate, Mean ± SD	74.75 ± 9.63	80.05 ± 9.70	−4.084	**0.000**
QT, Median (IQR)	378.00 (362.00, 398.00)	370.00 (356.00, 392.00)	−2.003	0.045
QTc interval, Median (IQR)	421.00 (411.00, 433.00)	430.00 (419.00, 437.00)	3.341	**0.001**
PR interval, Median (IQR)	148.00 (138.00, 162.00)	152.00 (140.00, 166.00)	1.199	0.230
Idiopathic QRS axis catheter ablation, Mean ± SD	33.10 ± 29.04	29.06 ± 26.81	1.076	0.283
QRS, Median (IQR)	80.00 (74.00, 84.00)	78.00 (74.00, 84.00)	−1.579	0.114
RV5+SV1, Mean ± SD	1.82 ± 0.54	1.73 ± 0.53	1.262	0.208

Note: Bold values indicate $P < 0.005$.

203 (83.5%), medium-risk 14 (5.8%), high-risk 21 (8.6%) and extreme high-risk 5 (2.1%). ASCVD risk stratification of premenopausal and postmenopausal breast cancer patients: the number of premenopausal breast cancer patients was significantly more than that of postmenopausal breast cancer patients in low-risk population, and the difference was statistically significant ($p < .05$). In moderate-risk and high-risk groups, the number of postmenopausal group was significantly higher than that of premenopausal group, and difference was statistically significant ($p < .05$) (Table 7).

ASCVD status of breast cancer patients after chemotherapy: ASCVD risk stratification in breast cancer patients after TEC chemotherapy: 183 (75.3%) patients had a low risk, 22 (9.1%) patients had a moderate, 33 (13.6%) patients had a high-risk and 5 (2.1%) patients had an extreme risk. The results showed after chemotherapy, the number of low-risk group decreased, the number of medium-risk group increased, the number of an extreme risk group did not change before and after chemotherapy, and there was no statistical difference. ASCVD risk stratification of premenopausal and postmenopausal breast cancer patients showed that the number of low-risk patients decreased and the number of medium-risk patients increased in the premenopausal group after chemotherapy, while in the post-menopausal group, the opposite trend was shown. In the low-risk patients, the number of premenopausal patients was significantly higher than that of post-menopausal patients, with statistical significance ($p < .05$). In the moderate-risk and high-risk groups, the number of postmenopausal group was significantly higher than that of premenopausal group, and the difference was statistically significant ($p < .05$).

3.6 | Effects of TEC chemotherapy regimen and cardiovascular risk factors on resting heart rate in breast cancer patients

Univariate analysis showed that age, menopausal status, hyperlipidaemia and carbonyldiamide level are the influencing factors of heart rate increase after chemotherapy for breast cancer patients. Binary logistics regression analysis showed that menopausal status ($p = .005$) is the risk factor for elevated heart rate. Patients with postmenopausal status were 0.47 times more likely to elevated heart rate than patients with premenopausal status (Table 8).

4 | DISCUSSION

Early detection and treatment of breast cancer can prolong survival. The leading cause of death in women with breast cancer is cardiovascular disease, not the tumour itself. This phenomenon was closely related to the common risk factors of the two diseases themselves (Rasmussen-Torvik et al., 2013), the toxicity of therapeutic drugs and clinicians identification and intervention of potential cardiovascular risks. This study investigated the effects of TEC chemotherapy regimens on cardiovascular outcomes in breast cancer patients before and after chemotherapy.

Breast cancer patients have remarkably higher risk of cardiovascular disease than the general population. Traditional risk factors of cardiovascular risk factors include hypertension, hyperlipidaemia, diabetes, overweight and obesity, and smoking. This study showed that the prevalence of hypertension in breast cancer patients was 25.1%, which was higher than that in Chinese adult women (Hu Shengshou et al., 2019). This result may be related to: breast cancer and hypertension have common pathophysiological pathways in inflammation, metabolic disorders and so on. This may be also linked to blocking and altering of apoptosis by hypertension (Hamet, 1996). But until now, the causal relationship between breast cancer and hypertension are not unclear. The incidence of hypertension in postmenopausal breast cancer patients was higher than that in premenopausal patients (33.33% versus 18.18%) and higher than that in other Asian countries (30.60%). After receiving TEC chemotherapy, there was no significant change in blood pressure levels between premenopausal group and postmenopausal group. The conclusion of this study is consistent with the results of Lifu (2015). Their study

TABLE 7 Changes of ASCVD in postmenopausal and premenopausal breast cancer patients before and after chemotherapy ($n = 243$)

Characteristics	All ($n = 243$) No.(%)	Premenopausal ($n = 304$) No.(%)	Postmenopausal ($n = 296$) No.(%)	T	p
Baseline condition					
Low-risk, n (%)	203 (83.5)	124 (93.9)[a]	79 (71.2)[b]	24.73	**0.000**
Medium-risk, n (%)	14 (5.8)	1 (0.8)[a]	13 (11.7)[b]		
High-risk, n (%)	21 (8.6)	6 (4.5)[a]	15 (13.5)[b]		
Extreme-risk, n (%)	5 (2.1)	1 (0.8)	4 (3.6)		
Post-treatment condition					
Low-risk, n (%)	183 (75.3)	117 (88.6)[a]	66 (59.5)[b]	30.10	**0.000**
Medium-risk, n (%)	22 (9.1)	3 (2.3)[a]	19 (17.1)[b]		
High-risk, n (%)	33 (13.6)	11 (8.3)[a]	22 (19.8)[b]		
Extreme-risk, n (%)	5 (2.1)	1 (0.8)	4 (3.6)		

Note: Bold values indicate $P < 0.005$.

TABLE 8 Univariate and bivariate logistic regression models of risk factors for increased heart rate (n = 243)

	Univariate				Multivariate			
	β	OR	95%CI	*p*-valve	β	OR	95%CI	*p*-valve
Cumulative measurement of anthracyclines	0.000	1	0.998–1.002	0.826				
Age	0.035	1.035	1.006–1.065	*0.018*	−0.001	0.999	0.957–1.042	0.945
Menopausal status	−0.782	0.457	0.268–0.780	*0.004*	−0.766	0.465	0.272–0.794	*0.005*
Hypertension	0.219	1.245	0.691–2.246	0.466				
Hyperlipidaemia	0.295	0.587	0.329–1.045	*0.070*	−0.403	0.668	0.368–1.214	0.186
LP (a)	0.000	1	0.999–1.002	0.441				
Type II Diabetes mellitus	0.178	1.195	0.261–5.463	0.818				
Hyperuricaemia	0.473	1.604	0.317–8.120	0.568				
Carbonyldiamide level	0.180	1.195	0.997–1.437	*0.054*	0.136	1.146	0.943–1.392	0.171
Creatinine level	0.005	1.005	0.982–1.029	0.685				
Overweight and obesity	−0.256	0.774	0.439–1.365	0.376				

Note: β, Regression coefficient.

Abbreviations: CI, confidence interval; OR, odds ratio.

Bold values indicate P < 0.005.

showed that there was no statistical difference in systolic and diastolic blood pressure between breast cancer patients whether received anthracycline chemotherapy or not. This result may be related to the minor damage effect of TEC chemotherapy regimen on vascular endothelium.

Hyperlipidaemia is a major risk factor for cardiovascular disease; people with hyperlipidaemia were double risk to develop cardiovascular disease than people with normal lipid levels. Studies showed that prevalence of hyperlipidaemia in healthy adults in China is greatly affected by menstrual status, and the prevalence has gradually increased from perimenopause (Cui Wenxin et al., 2014). However, in this study, among the first diagnosed breast cancer patients, the prevalence of hyperlipidaemia was significantly different between premenopausal and postmenopausal women (23.48% versus 40.54%, *p* < .05). Studies have found that high blood lipid level may initiate the pro-inflammatory signalling cascade reaction and cause chronic inflammation (Hovland et al., 2015), and inflammation is associated with the development of breast cancer. It is speculated that the occurrence of breast cancer in postmenopausal patients may be related to the early occurrence of hyperlipidaemia. It is suggested that postmenopausal breast cancer patients should be tested as early as possible. In addition, our study shows such a result that many indexes of blood lipid increased significantly after chemotherapy; the levels of blood lipids were in the direction of promoting atherosclerosis, and the prevalence of hyperlipidaemia also increased significantly (*p* < .05). Our research is consistent with the results of Tian et al. (2019) and Sharma et al. (2016) Therefore, we suggest that breast cancer patients receiving anthracycline-based chemotherapy should undergo rigorous lipid management, so as to prevent atherosclerotic disease. Further analysis found that there was no significant difference in TC and LDL-C levels in the menopausal group before and after chemotherapy, which was

different from the results of most studies (Sun et al., 2020). A meta-analysis by Touvier et al. (2015). showed that TC level was inversely correlated with the severity of breast cancer. The small change of LDL-C level after chemotherapy may be related to increased LDL-C receptor activity in malignant cells and lead to high uptake and high degradation of LDL-C (Vitols et al., 1985). It suggested that postmenopausal patients with breast cancer may be more serious than premenopausal patients, and breast cancer screening should be actively undertaken.

In our study, the prevalence rate of first diagnosed breast cancer with diabetes was 2.9% and that after chemotherapy was 6.6%. However, the prevalence of diabetes in Chinese women was 10.2% (Hu Shengshou et al., 2019). This may be related to the fact that people who have started diabetes medication are not included in the study population. Because patients do not routinely perform OGTT test, many breast cancer patients with latent diabetes or pre-diabetes are missed diagnosis, which is not conducive to the risk assessment, prognosis management and intervention of cardiovascular diseases. At the same time, it is suggested that people should pay attention to the fasting blood glucose level of breast cancer patients and actively carry out OGTT test screening at the beginning of diagnosis.

SUA is an important biomarker of cardiovascular disease. Apart from causing the deposition of urate crystals, hyperuricaemia may be involved in the pathophysiological processes of cardiovascular disease by impairing vascular endothelial function, stimulating oxidative stress, promoting platelet adhesion and altering haemorheology (Ndrepepa, 2018). We found that blood uric acid levels and the prevalence of hyperuricaemia were significantly increased after receiving anthracycline-based chemotherapy (*p* < .05). Moreover, uric acid changes were more prominent in premenopausal breast cancer patients, which was consistent with the study of Bu Hanli et al. (2020). It may be associated with transient or premature permanent

amenorrhoea in premenopausal patients with anthracycline chemotherapy. In other words, oestrogen has a decreased inhibitory effect on uric acid. Therefore, it is very necessary to strengthen the health management of hyperuricaemia in premenopausal breast cancer patients.

ASCVD risk stratification scheme recommended by Chinese Guidelines for Prevention and Treatment of Dyslipidemia. Through the comprehensive index data of age, diabetes, ASCVD history, blood lipid and so on, it establishes the mathematical model to predict the risk of ASCVD disease in the general population of China (Chu Junren et al., 2016). According to our study, the risk stratification of ASCVD in the first diagnosed breast cancer patients mainly had a low risk. The number of low-risk ASCVD patients after chemotherapy was significantly lower than that before chemotherapy. In addition to postmenopausal oestrogen protection of the body weakened, it can cause myocardial injury and lead to myocardial ischaemia by damaging the cardioprotective factor. When combined with traditional CVRF such as hypertension, hyperlipidaemia and diabetes, the protective effect of STAT3 will be weakened, making the myocardium more vulnerable to injury (Ferdinandy et al., 2014). In addition, lipid metabolism may indirectly increase the risk of ASCVD (Malarkodi et al., 2003). Therefore, ASCVD risk assessment should be actively given early in breast cancer patients, especially postmenopausal breast cancer patients.

Normally, resting heart rate (RHR) was negatively related to QTc prolongation. However, we found that QTc interval prolonged and RHR significantly accelerated after chemotherapy (76.20 ± 10.89 versus 80.32 ± 10.76, $p < .05$). Stachowiak et al. (2018) also found that RHR increased in breast cancer patients using anthracyclines. In our research, we also found that menopausal status may be major risk factors for increased RHR. Increased HR is a sign of abnormal autonomic nerve regulation and excessive sympathetic excitation of the circulatory system. Postmenopausal women are prone to autonomic dysfunction due to decreased oestrogen, and anticancer drugs such as anthracycline may damage the autonomic nervous system (Caru et al., 2019). A follow-up study of 4,980 breast cancer survivors in South Korea showed that breast cancer patients with a higher RHR had a poor prognosis, and RHR was positive related to FBG, TG level and BP level of breast cancer survivors (Lee et al., 2018). These factors may further exacerbate cardiovascular disease risk. Postmenopause is an independent risk factor for RHR increase, so we should pay more attention to cardiovascular status of these patients.

Although changes in the above indicators after chemotherapy can affect cardiovascular health, they belong to different departments of diseases. The management of DM, hyperlipidaemia and SUA may need the participation of endocrinology and nutrition departments. The management of HBP, ECG and ASCVD may require intervention from the cardiology department, and the use of chemotherapeutic agents requires the involvement of the medical oncology department. For a part of breast cancer patients, psychological counselling in the psychiatric department is also very important.

5 | STUDY LIMITATIONS

This is a single-centre study, and the sample size is not enough. Thus, the results may be biased and do not fully represent the results of real-world research.

6 | CONCLUSION

1. Compared with premenopausal patients, postmenopausal patients have more cardiovascular risk factors and higher risk of ASCVD at the initial diagnosis of breast cancer.
2. After chemotherapeutic, the levels of cardiovascular risk factors in both groups changed to pathogenic direction. Chemotherapeutic agents raised the risk of ASCVD in these patients, especially in the medium-risk population.
3. Postmenopausal breast cancer patients are more likely to have a faster resting heart rate after chemotherapy.

7 | IMPLICATIONS OF THE FINDINGS FOR NURSING RESEARCH AND PRACTICE

It is suggested that multidisciplinary cooperation should be strengthened, so as to promote dynamic cardiovascular fitness evaluation during the diagnosis and cure of breast cancer patients.

CONFLICTS OF INTEREST
The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS
Zhaoying Dong, Xiaoli Zhou: Designed the study. Zhaoying Dong, Zhaojun Liu, Siyu Chen, Jun Xiao: Collected the data. Zhaoying Dong, Changhong Zhang: Analysed the data. Zhaoying Dong, Xiaoli Zhou: Prepared the manuscript. All authors approved the final version for submission.

AUTHORSHIP STATEMENT
All listed authors meet the authorship criteria, and all authors are in agreement with the content of the manuscript.

ETHICAL APPROVAL
This study was a retrospective survey, and the patient's data were anonymous. The informed consent and ethical approval were not required.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Xiaoli Zhou https://orcid.org/0000-0002-3096-3911

REFERENCES

Bevers, T. B., Helvie, M., Bonaccio, E., Calhoun, K. E., Daly, M. B., Farrar, W. B., Garber, J. E., Gray, R., Greenberg, C. C., Greenup, R., Hansen, N. M., Harris, R. E., Heerdt, A. S., Helsten, T., Hodgkiss, L., Hoyt, T. L., Huff, J. G., Jacobs, L., Lehman, C. D., … Kumar, R. (2018). Breast cancer screening and diagnosis, version 3.2018, nccn clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network*, *16*(11), 1362–1389. https://doi.org/10.6004/jnccn.2018.0083

Bu Hanli, L. Z., Gao Xiuyin, L. U., Zhaojun, S. Y., & Yi, X. (2020). Effect of chemotherapy on blood lipid, blood glucose and uric acid in breast cancer patients and its factors. *Journal of Medical Research*, *49*, 145–149.

Caru, M., Corbin, D., Périé, D., Lemay, V., Delfrate, J., Drouin, S., Bertout, L., Krajinovic, M., Laverdière, C., Andelfinger, G., Sinnett, D., & Curnier, D. (2019). Doxorubicin treatments induce significant changes on the cardiac autonomic nervous system in childhood acute lymphoblastic leukemia long-term survivors. *Clinical Research in Cardiology*, *108*(9), 1000–1008. https://doi.org/10.1007/s00392-019-01427-9

Chen, C., Lu, F. C., & Department of Disease Control Ministry of Health, PR China (2004). The guidelines for prevention and control of overweight and obesity in Chinese adults. *Biomedical & Environmental Sciences Bes*, *17*(Suppl), 1–36. https://doi.org/10.1111/j.1365-2028.2008.00991.x

Chu Junren, G. R., Shuiping, Z., Dong, Z., & Jianjun, L. I. (2016). Guidelines for the prevention and treatment of dyslipidemia in Chinese adults (2016 Revision). *Chinese Circulation Journal*, *16*(10), 15–35. https://doi.org/10.3760/cma.j.issn.1671-7368.2017.01.006

Cui Wenxin, Z. X., Lijun, C., & Gengli, Z. (2014). Relationship between menstrual status and cardiovascular disease in perimenopausal women. *Journal of Cardiovascular and Cerebrovascular Diseases of Integrated Traditional Chinese and Western Medicine*, *12*, 519–521.

Ferdinandy, P., Hausenloy, D. J., Heusch, G., Baxter, G. F., & Schulz, R. (2014). Interaction of risk factors, comorbidities, and comedications with ischemia/reperfusion injury and cardioprotection by preconditioning, postconditioning, and remote conditioning. *Pharmacological Reviews*, *66*(4), 1142–1174. https://doi.org/10.1124/pr.113.008300

Hamet, P. (1996). Cancer and hypertension. *An Unresolved Issue. Hypertension*, *28*(3), 321–324. https://doi.org/10.1161/01.hyp.28.3.321

Harake, D., Franco, V. I., Henkel, J. M., Miller, T. L., & Lipshultz, S. E. (2012). Cardiotoxicity in childhood cancer survivors: Strategies for prevention and management. *Future Cardiology*, *8*(4), 647–670. https://doi.org/10.2217/fca.12.44

Herait, P., Poutignat, N., Marty, M., & Bugat, R. (1992). Early assessment of a new anticancer drug analogue–are the historical comparisons obsolete? The French experience with pirarubicin. *European Journal of Cancer*, *28*(10), 1670–1676. https://doi.org/10.1016/0959-8049(92)90066-b

Hovland, A., Jonasson, L., Garred, P., Yndestad, A., Aukrust, P., Lappegård, K. T., Espevik, T. & Mollnes, T. E. (2015). The complement system and toll-like receptors as integrated players in the pathophysiology of atherosclerosis. *Atherosclerosis*, *241*(2), 480–494.

Hu Shengshou, G. R., Lisheng, L., Manlu, Z., Wen, W., Wang Yongjun, W. U., Zhaosu, L. H., Dongfeng, G. U., Yuejin, Y., Zhe, Z., & Weiwei, C. (2019). Summary of China's cardiovascular report 2018. *Chinese Circulation Journal*, *34*(3), 6–17.

Lee, M. K., Lee, D. H., Park, S., Kim, S. I., & Jeon, J. Y. (2018). Relationship between resting heart rate and metabolic risk factors in breast cancer patients. *Clinica Chimica Acta*, *486*, 104–109. https://doi.org/10.1016/j.cca.2018.07.032

Lifu, Z. (2015). Effect of anthracycline-based chemotherapy on blood pressure and vascular endothelial function in supine position of breast cancer patients. Nanchang University.

Malarkodi, K. P., Balachandar, A. V., & Varlakshmi, P. (2003). The influence of lipoic acid on adriamycin-induced hyperlipidemic nephrotoxicity in rats. *Molecular and Cellular Biochemistry*, *247*(1–2), 139–145. https://doi.org/10.1023/a:1024175325850

McGowan, J. V., Chung, R., Maulik, A., Piotrowska, I., Walker, J. M., & Yellon, D. M. (2017). Anthracycline chemotherapy and cardiotoxicity. *Cardiovascular Drugs and Therapy*, *31*(1), 63–75. https://doi.org/10.1007/s10557-016-6711-0

Multi-Disciplinary Expert Task Force on Hyperuricemia and Its Related Diseases. (2017). Chinese multi-disciplinary consensus on the diagnosis and treatment of hyperuricemia and its related diseases. *Zhonghua Nei Ke Za Zhi*, *56*(3), 235–248. https://doi.org/10.3760/cma.j.issn.0578-1426.2017.03.021

Nakamae, H., Tsumura, K., Akahori, M., Terada, Y., Yamane, T., Hayashi, T., Saito, I., Kaneko, M., Okamoto, N., Ichihara, Y., Ohta, K., & Hino, M. (2004). QT dispersion correlates with systolic rather than diastolic parameters in patients receiving anthracycline treatment. *Internal Medicine*, *43*(5), 379–387. https://doi.org/10.2169/internalmedicine.43.379

Ndrepepa, G. (2018). Uric acid and cardiovascular disease. *Clinica Chimica Acta*, *484*, 150–163. https://doi.org/10.1016/j.cca.2018.05.046

Patnaik, J. L., Byers, T., DiGuiseppi, C., Dabelea, D., & Denberg, T. D. (2011). Cardiovascular disease competes with breast cancer as the leading cause of death for older females diagnosed with breast cancer: A retrospective cohort study. *Breast Cancer Research*, *13*(3), R64. https://doi.org/10.1186/bcr2901

Qi, Y. (2018). 2018 Chinese guideline on menopause management and menopause hormone therapy. *Medical Journal of Peking Union Medical College Hospital*, *9*(6), 512–525. https://doi.org/10.3760/cma.j.issn.0529-567x.2018.11.001

Rasmussen-Torvik, L. J., Shay, C. M., Abramson, J. G., Friedrich, C. A., Nettleton, J. A., Prizment, A. E., & Folsom, A. R. (2013). Ideal cardiovascular health is inversely associated with incident cancer: The atherosclerosis risk in communities study. *Circulation*, *127*(12), 1270–1275. https://doi.org/10.1161/circulationaha.112.001183

Sharma, M., Tuaine, J., McLaren, B., Waters, D. L., Black, K., Jones, L. M., & McCormick, S. P. (2016). Chemotherapy agents alter plasma lipids in breast cancer patients and show differential effects on lipid metabolism genes in liver cells. *PLoS One*, *11*(1), e0148049. https://doi.org/10.1371/journal.pone.0148049

Stachowiak, P., Milchert-Leszczynska, M., Falco, M., Wojtarowicz, A., Kaliszczak, R., Safranow, K., & Kornacewicz-Jach, Z. (2018). Heart rate variability during and after chemotherapy with anthracycline in patients with breast cancer. *Kardiologia Polska*, *76*(5), 914–916. https://doi.org/10.5603/kp.2018.0098

Sun, X. Y., Ma, F., Tian, P. F., Li, X. S., Zhu, A. H., Wang, J. J., & Liu, B. L. (2020). The metabolism of blood glucose and lipid in breast cancer patients after the first chemotherapy. *Zhonghua Zhong Liu Za Zhi*, *42*(7), 580–585.

The DECODE study group on behalf of the Europe an Diabetes Epidemiology Group. (1999). Glucose tolerance and mortality: Comparison of WHO and American Diabetes Association diagnostic criteria. The DECODE study group. European Diabetes Epidemiology Group. Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe. *Lancet*, *354*(9179), 617-621.

Tian, W., Yao, Y., Fan, G., Zhou, Y., Wu, M., Xu, D., & Deng, Y. (2019). Changes in lipid profiles during and after (neo)adjuvant chemotherapy in women with early-stage breast cancer: A retrospective study. *PLoS One*, *14*(8), e0221866. https://doi.org/10.1371/journal.pone.0221866

Touvier, M., Fassier, P., His, M., Norat, T., Chan, D. S., Blacher, J., Hercberg S., Galan P., Druesne-Pecollo N., & Latino-Martel P. (2015). Cholesterol and breast cancer risk: A systematic review and meta-analysis of prospective studies. *British Journal of Nutrition*, *114*(3), 347–357.

Vitols, S., Gahrton, G., Bjorkholm, M., & 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*, *2*(8465), 1150–1154. https://doi.org/10.1016/s0140-6736(85)92679-0

Williams, B., Mancia, G., Spiering, W., Agabiti Rosei, E., Azizi, M., Burnier, M., Clement, D. L., Coca, A., de Simone, G., Dominiczak, A., Kahan, T., Mahfoud, F., Redon, J., Ruilope, L., Zanchetti, A., Kerins, M., Kjeldsen, S. E., Kreutz, R., Laurent, S., … Desormais, I. (2018). 2018 ESC/ESH Guidelines for the management of arterial hypertension: The task force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The task force for the management of arterial hypertension of the European Society of Cardiology and the European Society of hypertension. *Journal of Hypertension*, *36*(10), 1953–2041. https://doi.org/10.1097/hjh.0000000000001940