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Original Article

Cardiovascular disease risk factors among transgender women in Chiang Mai, Thailand

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Abstract: Transgender individuals take hormone therapy (HT) for transitioning secondary sexual characteristics, especially by transgender women assigned male at birth (AMAB). The transgender drug is a relatively new field in health care, but limited data exist to inform the cardiovascular risk factor profile among younger individuals undergoing HT. Therefore, this study was to evaluate the relationship between HT and cardiovascular (CVD) risk factors in Thai transgender women. A cross-sectional study was conducted from October 1st 2018-November 30th 2018 in 100 transgender women not receiving HT (Control group) and 100 transgender women receiving HT (HT group) in Chiang Mai, Thailand. Demographic data were recorded for each consenting subject. Non-invasive arterial examinations were undertaken, including carotid intima-media thickness (CIMT), ankle-brachial index (ABI), and cardio-ankle vascular index (CAVI). CVD risk factors including lipid profiles, fasting plasma glucose (FPG), C-reactive protein (CRP), cardiovascular risk markers (pro b-type natriuretic peptide (proBNP) and cardiac troponin I), and sex hormone levels were determined. The average age in both groups was 24±5.1 years. The average time of HT use was 6.65±0.52 years in the HT group. Mean waist circumference was significantly lower in the HT group compared with the control group (77.50±14.00 *vs.* 81.20±12.90 cm; P=0.004) while CRP (3.44±6.82 *vs.* 3.28±5.80 mg/L; P=0.031) and cardiac troponin I (0.029±0.051 *vs.* 0.014±0.014 ng/mL; P=0.040) values were greater in HT group than the control group. Mean CIMT was lower in the HT group *vs.* the control group (P=0.094). Among transgender women, receiving HT was associated with enhanced levels of a subset of CVD risk factors. More research is necessary to inform the need for novel CVD prevention and treatment strategies in transgender women.

Keywords: Cardiovascular disease, transgender women, hormone therapy

Introduction

In the general population, cisgender men have greater rates of cardiovascular pathology compared to cisgender women until reaching 65-75 years of age, and-these differences are believed to be related in part to the hormone-related effects of estrogen and testosterone. The impact of hormones on CVD and CVD risk factors in transgender people are poorly understood [1].

Transgender individuals take hormone therapy (HT) for transitioning secondary sexual characteristics. One of the most severe known adverse drug reactions of HT besides venous thromboembolism is a cardiovascular disease; nevertheless, there is restricted understanding about the long-term impact of this gender-affirming hormone therapy on cardiovascular health in transgender women and transgender men. A vast majority of transgender women use cross-sex hormones to reduce male sex hormones and supplement female sex hormones. These treatments have side effects that may include thromboembolism and coronary heart disease. In transgender adults, HT has been associated with the likely for impairment CVD risk factors [2].

Previous studies on long-term effects and adverse effects of HT in both transgender men and women demonstrated that HT appears to be safer in transgender men than in transgen-

der women. Transgender women experienced thromboembolic and other cardiovascular incidences in hormone treatment [3], and oral estrogens increase the risk for cardiovascular disease mortality and triglyceride levels in transgender women individuals receiving long-term HT [2, 4]. Moreover, HT in transgender women showed an increasing prevalence of myocardial infarction, cerebrovascular disease, hyperprolactinemia, type 2 diabetes, and thromboembolic effects with estrogens. Both testosterone and estrogens derivatives could induce liver dysfunction [5, 6]. Thailand has a large and diverse transgender community, especially transgender women assigned male at birth (AMAB). The cardiac troponin I and pro b-type natriuretic peptide (proBNP) are widely used as diagnostic biomarkers for cardiovascular disease. However, no study focused on this point in transgender women receiving hormone therapy in Thailand is available. A recent study reported that a low dose of hormone self-medication use by young Thai transgender women showed no severe risk of cardiovascular disease [7]. There are some restrictions in the study, including short follow-up, small sample size, weaker the study design, and its limitations. Therefore, they suggested that the studies with longer follow-ups and a more sturdy design would encourage to explain this problem further.

However, the knowledge about both traditional and unique CVD risk factors in transgender women receiving HT in Thailand is still lacking. Therefore, the study aims to elucidate CVD risk factors in the transgender women receiving HT in Chiang Mai, Thailand. To fill out the gap of the limited knowledge of the association between CVD and HT and make the awareness in transgender women.

Materials and methods

Participants

A cross-sectional study was performed in 200 transgender populations, attending the PIMAN Center, Chiang Mai, Thailand, and between October 2018 and November 2018. The study was approved by the Human Experimental Committee, Research Institute for Health Sciences (RIHES), Chiang Mai University, Chiang Mai, Thailand (Project No. 10/61), and all transgender women gave their informed consent. Inclusion criteria in this willing study included healthy transgender women or men more than 18 years old who could comply with the research protocol and were willing to give informed consent. Participants encountering from any violent or chronic diseases were excluded from the study.

Data collection

Demographic data were recorded for each consenting subject, including age, sexual and behavioral characteristics, smoking status, alcohol consumption, psychosocial aspects, and hormonal use, using a questionnaire and face-to-face interview. Physical examination included determination of body mass index (BMI), weight, height, waist circumference, systolic and diastolic blood pressure, and heart rate. Non-invasive arterial examinations for cardiovascular disease were performed using a vascular screening device, model VaSera™ VS-1500N (FUKUDA DENSHI Co., Ltd., Tokyo, Japan), including cardio-ankle vascular index (CAVI), pulse wave velocity (PWV), and ankle-brachial index (ABI) to evaluate subclinical atherosclerosis (defined as CAVI > 9.0 and PWV > 13 m/s) and peripheral arterial disease (defined as ABI < 0.9) [8, 9], respectively. Furthermore, carotid intima-media thickness (CIMT) was measured using a SonoScape X3 portable Doppler ultrasound (Guangzhou Medsinglong Medical Equipment Co., Ltd., Guangzhou, China) which high-resolution B-mode ultrasound measurement was applied. The mean value of CIMT was determined at the distal common carotid artery (CCA) (1 cm proximal to the carotid bifurcation) at the far wall [10], to determine the risk of a cardiovascular event (defined as CIMT > 1.0 mm) [11].

After fasting overnight for 10-12 hours, the blood sample was collected via venipuncture was used to determine lipid profiles including HDL-cholesterol, direct LDL-cholesterol, triglyceride, and total cholesterol, fasting plasma glucose (FPG) (RX Daytona, i+MED Laboratories Company Limited., Thailand), C-reactive protein (CRP; Merck, CYT298, USA), cardiovascular risk markers including cardiac troponin I (Abcam, ab200016, UK) and pro b-type natriuretic peptide (proBNP; Abcam, ab193712, UK), and sex hormone levels including testosterone (Abcam, ab174569, UK) and 17-beta estradiol (Abcam,

Table 1. Demographic and baseline characteristics of transgender women

Characteristics	Control group (N=100)	HT group (N=100)	*P*-value
Age (years)	24.3±5.7	24.0±5.1	0.669
BMI (kg/m^2)	23.10±4.60	22.50±5.00	0.134
Waist circumference (cm)	81.20±12.90	77.50±14.00	0.004*
Smoking status, N (%)			0.553
Never or former	83 (83)	87 (87)	
Current	16 (16)	13 (13)	
Other	1 (1)	-	
Alcohol drinking, N (%)			0.171
Never or former	19 (19)	12 (12)	
Current	81 (81)	88 (88)	
Exercise, N (%)			0.007*
No	36 (36)	55 (55)	
Yes	64 (64)	45 (45)	
Duration of hormone therapy (years)		6.65±0.52	

N: number; BMI: body mass index. Data presented as mean ± SD. *P-value < 0.05 was considered statistically significant.

Table 2. CVD first factors among those taking HT and those who are not taking HT

Cardiovascular Risk	Control group (N=100)	HT group (N=100)	*P*-value
Systolic blood pressure (mmHg)			
Model 1	127.79±1.18	126.73±1.18	0.5253
Model 2	127.75±1.61	126.83±1.62	0.7390
Model 3	127.67±1.40	126.91±1.41	0.7551
Diastolic blood pressure (mmHg)			
Model 1	76.91±0.92	77.3±0.92	0.7578
Model 2	77.00±1.13	77.33±1.14	0.8655
Model 3	76.77±1.09	77.57±1.10	0.6720
Heart rate (bmp)			
Model 1	67.69±1.31	71.98±1.31	0.0212*
Model 2	67.85±1.77	71.82±1.79	0.1980
Model 3	68.32±1.79	71.35±1.81	0.3335
Pulse wave velocity (m/s)			
Model 1	9.46±0.35	8.77±0.37	0.1732
Model 2	9.50±0.45	8.67±0.50	0.3097
Model 3	9.53±0.47	8.63±0.52	0.2975
ABI			
Model 1	1.05±0.009	1.03±0.009	0.0677
Model 2	1.05±0.01	1.04±0.01	0.8733
Model 3	1.04±0.012	1.05±0.012	0.7886
CAVI			
Model 1	6.17±0.10	6.48±0.10	0.0274*
Model 2	6.25±0.12	6.40±0.13	0.4893
Model 3	6.29±0.12	6.37±0.12	0.6992
CIMT (mm)			

ab108667, UK) were determined using an enzyme-linked immunosorbent assay (ELISA). Plates were read on a SPECTROstar® *Nano* microplate reader (BMG LABTECH, Germany).

Statistical analysis

All statistical analyses have carried on with the program SAS for Windows version 9.4 (SAS Institute, Cary, USA). Descriptive for continuous variables were presented using the mean ± standard deviation (SD) or the mean ± standard error (SE) and analyzed with the T-test/ Mann Whitney U test. Fisher's exact test or Chi-square test was used in the comparison of categorized variables. Multivariable linear regression models regressed CVD risk factors on HT status. Among the subgroup of HT users, we estimated the relationship between duration of use and CVD risk factors. Multivariable models included age, gender, education, income, alcohol drinking, smoking, exercise, and BMI. The *P*-value < 0.05 was considered statistically significant.

Results

Demographic and baseline characteristics of transgender women were shown in **Table 1**. The average ages of transgender women receiving HT and controls were 24.0±5.1 and 24.3±5.7 years old (P=0.67). There was no statistical variation in age, BMI, smoking

Model 1	0.377±0.0070	0.348±0.0070	0.0031*
Model 2	0.378±0.0092	0.346±0.0093	0.0414*
Model 3	0.376±0.0095	0.348±0.0095	0.0943
Lipid profiles			
Total cholesterol (mg/dL)			
Model 1	206.13±3.86	206.28±3.86	0.9781
Model 2	206.74±5.27	206.13±5.31	0.9463
Model 3	207.76±5.41	205.10±5.45	0.7771
Triglyceride (mg/dL)			
Model 1	100.73±5.90	103.87±5.90	0.7071
Model 2	104.62±7.57	99.78±7.62	0.7111
Model 3	106.16±7.37	98.22±7.42	0.5347
HDL (mg/dL)			
Model 1	50.14±1.28	56.43±1.28	0.0006*
Model 2	51.41±1.79	55.29±1.80	0.2098
Model 3	51.64±1.69	55.06±1.70	0.2440
LDL (mg/dL)			
Model 1	137.88±4.10	132.16±4.10	0.3245
Model 2	137.21±5.70	133.22±5.74	0.6847
Model 3	135.97±5.69	134.47±5.73	0.8791
FPG (mg/dL)			
Model 1	97.82±2.61	98.05±2.61	0.9504
Model 2	95.68±3.41	100.28±3.44	0.4345
Model 3	96.44±3.45	99.52±3.48	0.6079
CRP (mg/L)			
Model 1	3.28±0.63	3.44±0.63	0.8635
Model 2	3.23±0.88	3.52±0.89	0.8489
Model 3	2.96±0.88	3.79±0.89	0.5909
Cardiac troponin I (ng/mL)			
Model 1	0.01±0.004	0.03±0.004	0.0035*
Model 2	0.02±0.005	0.02±0.005	0.5366
Model 3	0.02±0.005	0.02±0.005	0.8811
pro BNP (pg/mL)			
Model 1	0.002±0.0002	0.002±0.0002	0.5636
Model 2	0.002±0.0003	0.002±0.0003	0.7452
Model 3	0.002±0.0003	0.002±0.0004	0.9118
Testosterone (ng/mL)			
Model 1	6.37±0.23	4.30±0.23	< 0.0001*
Model 2	5.89±0.30	4.77±0.30	0.0321*
Model 3	5.81±0.30	4.84±0.30	0.0635
17-beta estradiol (pg/mL)			
Model 1	30.47±10.43	49.50±10.43	0.1984
Model 2	34.74±14.79	45.60±14.91	0.6725
Model 3	34.74±14.79	45.60±14.91	0.6725

Model 1: Crude. Model 2: Adjusting for age, gender, education, and income. Model 3: Adjusting for age, gender, education, income, alcohol drinking, smoking, exercise, and BMI. N: number; ABI: ankle-brachial index; BMI: body mass index; CAVI: cardio-ankle vascular index; CIMT: carotid intima-media thickness; HDL: high-density lipoprotein; LDL: low-density lipoprotein; FPG: fasting plasma glucose; CRP: C-reactive protein; pro BNP: pro b-type natriuretic peptide. All data presented as mean ± SE. *P-value < 0.05 was considered statistically significant.

status, and alcohol consumption between the HT group and the control group. However, we found that waist circumference was remarkably higher in the control group than the HT group (P= 0.004), and the HT group reported a higher popularity of exercise (P= 0.007). The duration of transgender women treated with HT therapy was 6.65±0.52 years.

Cardiovascular biomarker risk factors were demonstrated in **Table 2**. The HT group showed statistically significantly higher levels of HDL-cholesterol (56.43±1.28 mg/dL, P=0.0006) and cardiac troponin 1 (0.03±0.004 ng/mL, P=0.0035) than in those control group. However, there are no variations in total cholesterol, triglycerides, LDL-cholesterol, FPG, CRP, or proBNP between the two groups were observed. To evaluate the levels of sex hormone, testosterone, and 17-beta estradiol were quantified. CIMT was modestly lower among the HT group *vs.* the control group (0.348± 0.0070 *vs.* 0.377±0.0070 mm, P=0.0031). As expected, testosterone was significantly more in the control group than in those HT group (6.37±0.23 *vs.* 4.30±0.23 ng/mL, P < 0.0001). However, there was no statistical variation in 17-beta estradiol levels between the two study groups.

Among HT users, for every 1-year increase in du-

Table 3. Modeling hormone duration and CVD risks including only those who were taking HT

Cardiovascular Risk	Parameter Estimate HT group (N=100)	*P*-value
Systolic blood pressure (mmHg)		
Model 1	0.211±0.223	0.3509
Model 2	-0.156±0.363	0.6674
Model 3	0.057±0.323	0.8600
Diastolic blood pressure (mmHg)		
Model 1	0.617±0.167	0.0004
Model 2	0.266±0.270	0.3270
Model 3	0.382±0.273	0.1647
Heart rate (bmp)		
Model 1	-0.055±0.191	0.7745
Model 2	0.087±0.312	0.7799
Model 3	0.165±0.323	0.6100
Pulse wave velocity (m/s)		
Model 1	0.064±0.056	0.2560
Model 2	0.085±0.109	0.4401
Model 3	0.099±0.121	0.4169
ABI		
Model 1	-0.0003±0.001	0.8268
Model 2	-0.006±0.002	0.0054*
Model 3	-0.006±0.002	0.0087*
CAVI		
Model 1	0.024±0.021	0.2526
Model 2	-0.056±0.031	0.0797
Model 3	-0.053±0.032	0.1045
CIMT (mm)		
Model 1	0.002±0.001	0.1867
Model 2	-0.001±0.002	0.4876
Model 3	-0.001±0.002	0.6025
Lipid profiles		
Total cholesterol (mg/dL)		
Model 1	0.014±0.683	0.9835
Model 2	-2.995±1.059	0.0058*
Model 3	-2.360±1.096	0.0341*
Triglyceride (mg/dL)		
Model 1	3.175±1.116	0.0054
Model 2	-0.067±1.803	0.9705
Model 3	0.268±1.836	0.8845
HDL (mg/dL)		
Model 1	0.228±0.250	0.3632
Model 2	0.528±0.418	0.2092
Model 3	0.348±0.400	0.3863
LDL(mg/dL)		
Model 1	-1.039±0.740	0.1634
Model 2	-3.895±1.161	0.0012*
Model 3	-3.076±1.182	0.0109*

ration of HT use, the results showed that ABI decreased by -0.006± 0.002, *P*=0.0054 while FPG increased by 2.681±0.543 mg/dL, *P* < 0.0001 (**Table 3**), total cholesterol decreased by -2.995±1.059, *P*= 0.0058 mg/dL, and LDL-cholesterol decreased by -3.895±1.161, *P*= 0.0012 mg/dL.

Discussion

Thailand has a large and diverse transgender community, especially transgender women assigned male at birth (AMAB). Many transgender persons in Thailand choose to use hormone therapy (HT), especially by transgender women for feminization. Transgender drug is a relatively new field in health care, but working with limited evidence about the impacts of HT. It has been found that some supplement gender-affirming hormones may have adverse effects, resulting in blockage of the veins and coronary heart disease. Previous reports showed the event of venous thromboembolism was low in transgender women taking oral estradiol in the United States [12], and 6% of transgender women experienced CVD troubles after, on average, 11.3 years of hormone therapy [3]. Some studies explored the effects of HT on transgender women. It was found that HT decreases the CVD cholesterol risk profile among transgender women after 1.5 years of HT [13].

Various determinants may promote to an enhancement of CVD in transgender women, including more rates of tobacco use, lipid disorders, reduced physical activity, obesity, and diabetes [5]. Unfortunately, limited information exists about CVD risk factors in transgender persons receiving HT in Thailand. Decreasing of CVD risk factors such as diabetes, hypertension, and tobacco use remains crucial in preventing CVD in transgender populations.

FPG (mg/dL)		
Model 1	2.681±0.543	<0.0001*
Model 2	2.227±0.868	0.0119*
Model 3	2.558±0.899	0.0055*
CRP (mg/L)		
Model 1	0.049±0.132	0.7138
Model 2	0.060±0.222	0.7878
Model 3	0.0862±0.222	0.6981
Cardiac troponin I (ng/mL)		
Model 1	-0.001±0.001	0.4651
Model 2	-0.001±0.002	0.5435
Model 3	-0.001±0.002	0.4256
pro BNP (pg/mL)		
Model 1	0.000003±0.00006	0.9632
Model 2	-0.0001±0.0001	0.1702
Model 3	-0.0002±0.0001	0.1029
Testosterone (ng/mL)		
Model 1	-0.069±0.054	0.2059
Model 2	-0.059±0.085	0.4911
Model 3	-0.044±0.085	0.6066
17-beta estradiol (pg/mL)		
Model 1	-0.491±2.841	0.8631
Model 2	-0.471±4.704	0.9204
Model 3	-0.437±4.917	0.9294

Model 1: Crude. Model 2: Adjusting for age, gender, education, and income. Model 3: Adjusting for age, gender, education, income, alcohol drinking, smoking, exercise, and BMI. ABI: ankle-brachial index; BMI: body mass index; CAVI: cardio-ankle vascular index; CIMT: carotid intima-media thickness; HDL: high-density lipoprotein; LDL: low-density lipoprotein; FPG: fasting plasma glucose; CRP: C-reactive protein; pro BNP: pro b-type natriuretic peptide. All data presented as a parameter estimate ± SE. *P-value < 0.05 was considered statistically significant.

Previous studies in transgender women revealed that the quantity of HDL-cholesterol in transgender women treated with estrogen was remarkably greater than in untreated transgender women. However, on the other hand, the PWV was decreased considerably in transgender women treated with estrogen compared to that in untreated transgender women [14]. CIMT as an early predictor of CVD and stroke incidences. It relates with various known risk factors for heart disease and the risk of future CVD incidences [15]. Darabian and colleagues [11] found that age, gender, HDL-cholesterol, diabetes, smoking, and hypertension had an important relation to the CIMT, which every 0.1 mm increase in the CIMT was correlated with a 10-15% increase in the venture of myocardial infarction. The decreasing value of CIMT in the HT group may be caused by estrogen receiving. Many shreds of evidence reported that estrogen is protective against the development of CVD in women [16, 17].

The limitation of the study is a small sample size. Notwithstanding, the results of the present study will provide baseline data for developing disease burden mitigation strategies to prolong life and relieve the risk factors of CVD in transgender women who were receiving HT. We would want this to be an initial pilot cohort that leads to a larger cohort of individuals to follow for several years to investigate CVD risk levels and trends in more detail.

Conclusions

The present study demonstrated no severe risk of health problems with HT use in transgender women. Also, HT therapy is likely to have some positive effects on carotid artery wall in transgender women.

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Disclosure of conflict of interest

None.

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References

[1] Gooren LJ, Wierckx K and Giltay EJ. Cardiovascular disease in transsexual persons treated with cross-sex hormones: reversal of the traditional sex difference in cardiovascular disease pattern. Eur J Endocrinol 2014; 170: 809-819.

[2] Streed CG Jr, Harfouch O, Marvel F, Blumenthal RS, Martin SS and Mukherjee M. Cardiovascular disease among transgender adults receiving hormone therapy: a narrative review. Ann Intern Med 2017; 167: 256-267.

[3] Wierckx K, Mueller S, Weyers S, Van Caenegem E, Roef G, Heylens G and T'Sjoen G. Long-term evaluation of cross-sex hormone treatment in transsexual persons. J Sex Med 2012; 9: 2641-2651.

[4] Maraka S, Singh Ospina N, Rodriguez-Gutierrez R, Davidge-Pitts CJ, Nippoldt TB, Prokop LJ and Murad MH. Sex steroids and cardiovascular outcomes in transgender individuals: a systematic review and meta-analysis. J Clin Endocrinol Metab 2017; 102: 3914-3923.

[5] Wierckx K, Elaut E, Declercq E, Heylens G, De Cuypere G, Taes Y, Kaufman JM and T'Sjoen G. Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: a case-control study. Eur J Endocrinol 2013; 169: 471-478.

[6] Bourgeois AL, Auriche P, Palmaro A, Montastruc JL and Bagheri H. Risk of hormonotherapy in transgender people: literature review and data from the French Database of Pharmacovigilance. Ann Endocrinol (Paris) 2016; 77: 14-21.

[7] Onpanna P, Daosodsai P, Leelawat K and Porasuphatana S. Cross-sex hormone use does not increase cardiovascular risk in young male-to-female transsexuals: a study of self-medication by healthy Thai cabaret dancers. Asian Biomedicine 2015; 9: 511-518.

[8] Sun CK. Cardio-ankle vascular index (CAVI) as an indicator of arterial stiffness. Integr Blood Press Control 2013; 6: 27-38.

[9] Miyatani M, Masani K, Oh PI, Miyachi M, Popovic MR and Craven BC. Pulse wave velocity for assessment of arterial stiffness among people with spinal cord injury: a pilot study. J Spinal Cord Med 2009; 32: 72-78.

[10] Timóteo AT, Mota Carmo M, Soares C and Ferreira RC. Has carotid intima-media thickness prognostic impact in patients with high cardiovascular risk? A long-term cohort study. Echocardiography 2019; 36: 125-132.

[11] Darabian S, Hormuz M, Latif MA, Pahlevan S and Budoff MJ. The role of carotid intimal thickness testing and risk prediction in the development of coronary atherosclerosis. Curr Atheroscler Rep 2013; 15: 306.

[12] Arnold JD, Sarkodie EP, Coleman ME and Goldstein DA. Incidence of venous thromboembolism in transgender women receiving oral estradiol. J Sex Med 2016; 13: 1773-1777.

[13] The effects of sex hormones on cardiovascular disease risk factors among transgender men and women undergoing hormone therapy on Philadelphia. https://www.mazzonicenter.org/trans-health/workshop/effects-sex-hormones-cardiovascular-disease-risk-factors-among-transgender-men. Accessed 23 November 2017.

[14] Sharula, Chekir C, Emi Y, Arai F, Kikuchi Y, Sasaki A, Matsuda M, Shimizu K, Tabuchi K, Kamada Y, Hiramatsu Y and Nakatsuka M. Altered arterial stiffness in male-to-female transsexuals undergoing hormonal treatment. J Obstet Gynaecol Res 2012; 38: 932-940.

[15] Sigurdsson FA. Carotid Intima-Media Thickness (CIMT). https://www.docsopinion.com/carotid-intima-media-thickness. Accessed 17 May 2019.

[16] Iorga A, Cunningham M. C, Moazeni S, Ruffenach G, Umar S and Eghbali M. The protective role of estrogen and estrogen receptors in cardiovascular disease and the controversial use of estrogen therapy. Biol Sex Differ 2017; 8: 33.

[17] Queen Mary, University of London. How estrogen could help protect women from cardiovascular disease. https://www.sciencedaily.com/releases/2011/08/110811181716.htm. Accessed 10 July 2019.