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Epidemiology of cardiovascular risk factors in two population-based studies☆

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A B S T R A C T

We aimed to compare cardiovascular risk factors prevalence in Italy and Russia through cross-sectional database analysis.

The study has been based on data from ESSE-RF and from baseline of PLIC study, two population-based epidemiological studies aimed to investigate prevalence of risk factors and evaluating contribution of traditional and new risk factors into morbidity and cardiovascular mortality.

A total of 2203 patients with left and right intima-media thickness (IMT) measurements constituted the source population (1205 from PLIC study and 998 from ESSE-RF study). Sample of ESSE-RF study had slightly more diabetic and hypertensive individuals, while the percentage of subjects with high cholesterol value was lower than in the other sample (67.1% vs 79.9%). The median LDL-C value was higher among individuals not treated with statins in the PLIC sample ($p < 0.001$), while was comparable among subjects receiving statin therapy. On the other hand, the percentage of individuals with positive cardiovascular history was higher in ESSE-RF sample. This could also explain the higher mean IMT value (0.71 ± 0.17 vs 0.63 ± 0.13) in the whole sample, and among patients without past cardiovascular events (regardless of statin treatment), despite some differences in major risk factors.

Despite Russian and Italian populations are culturally and geographically different, they are not so different based on characteristics analyzed.

1. Introduction

Cardiovascular diseases (CVD) remain the world leading cause of death [1]. Novel risk markers associated with cardiovascular risk are still wanted to promote better CVD prevention strategies, especially in intermediate and high risk groups. Vascular damage can be an important additional risk determinant as well as new biomarkers. Majority of studies evaluating risk factors and assessing new biomarkers are local and based on rather small sample studies and concentrate on the measurements of few biomarkers simultaneously, that do not let to generalize these results to the whole population because of geographical, ethnic and social discrepancies as well as do not allow to calculate predictive values in large models.

Being one of the important markers of subclinical vascular damage, intima-media thickness (IMT) evaluation can improve absolute risk assessment for CVD [2]. Moreover, the association between cardiovascular events and IMT was significant even after an adjustment for traditional risk factors [3]. According to the Rotterdam study, where 8 thousand patients over 55 years old participated, an association between the carotid IMT and damage of coronary arteries was found, that allowed to consider IMT as a

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predictor of high cardiovascular risk [4]. In a populational study of 3580 people without diabetes and CVD, the prognostic significance of IMT in addition to traditional risk factors (according to the Framingham scale) in 55–75 years old women was demonstrated. It gave an option of reclassification of patients from the low-risk in a high-risk group [5].

However, there is a list of factors, that makes IMT assessment complicated, among them aging is the most important. The annual increase in average IMT in the common carotid artery even in healthy individuals is 0.010 mm [6], that is a normal process and also observed in the absence of atherosclerosis. IMT increases in high blood pressure (BP) [7] as well as in any kind of chronic inflammation (rheumatoid diseases, diabetes, chronic obstructive pulmonary disease) [8], what can explain increased cardiovascular risk in these subgroups, which is not included in standard risk classifications. Besides, IMT and vascular damage can explain ethnic discrepancies in cardiovascular risk, while studies comparing different populations are lacking.

The present study was aimed to compare cardiovascular risk factors prevalence in Italy and Russia through cross-sectional database analysis.

2. Methods

2.1. Participants

The study has been based on data from ESSE-RF and from baseline of PLIC study.

ESSE-RF (Epidemiology of cardiovascular diseases in different regions of Russia) is a cross-sectional study in 13 Russian regions aiming at investigating prevalence of risk factors and evaluating contribution of traditional and new risk factors into morbidity and cardiovascular mortality in the population of Russian Federation. As a Saint-Petersburg part of this study 1600 apparently healthy participants aged 25–65 years were randomly selected in 2012. All participants signed informed consent and filled in the questionnaire regarding risk factors, concomitant diseases and therapy, range of laboratory tests, including fasting lipids and glucose (Abbott Architect 8000).

PLIC (Progression of the Intima Carotid Lesions) study is an ongoing observational, cross-sectional and longitudinal study of subjects enrolled on a voluntary basis in 1998–2000. The study was conducted by the Center for the Study of Atherosclerosis of Bassini Hospital (Cinisello Balsamo, Milan) in coordination with the Epidemiology and Preventive Pharmacology Centre (SEFAP) of the University of Milan. Subjects enrolled in the study undergo periodic visits to collect data about patient-reported personal and familial pathological history, lifestyle habits, clinical parameters, and drug therapies, together with blood sample to measure lipid and glycaemic profiles.

A sample of subjects, aged 25–65 years old, without missing values for IMT measurements, was selected from both the cohorts.

2.2. Assessments of IMT

In ESSE-RF study, measurement of intima-media thickness was performed by the portable diagnostic system My Sono U6 (Samsung, Korea). The standard protocol included measurements bilaterally at a distance of 1 cm from bifurcation of the common carotid artery along its posterior wall in three positions (anterior, middle and posterior longitudinal). The IMT was defined as the distance between the first and second echogenic line of the arthery. Then, the mean IMT on both sides was calculated as an arithmetic mean of three dimensions. In PLIC study, a B-mode ultrasound of carotid was performed to measure the mean IMT with the same technique already described. In both samples, the presence or absence of atherosclerotic plaques has been also estimated. The subclinical vascular damage was detected if IMT>0,9 mm. Local thickening ≥1.3 mm was regarded as atherosclerotic plaque.

2.3. Measurements and data analysis

The comparison analysis between samples was based on demographic information, body mass index (BMI), smoking, blood pressure as well as on lipid profile and glucose level. Antidiabetic, antihypertensive and statin therapies were also evaluated. In both samples, the prevalence of type 2 diabetes mellitus, hypertension and dyslipidemia were defined in case of self-reported specific drug use or biochemical/vital parameters with levels higher than the cut off for the diagnosis (140 mm Hg for systolic BP or/and 90 mm Hg for diastolic BP, 3.0 mmol/L for low-density lipoprotein cholesterol (LDL-C), and 7.0 mmol/L for glucose). Positive cardiovascular history was also defined based on self-reported history of stroke, myocardial infarction, coronary heart disease, angina, arrhythmia, or other heart diseases.

A comparison of mean IMT (arithmetic mean of left and right-side measurements) trends at baseline has been also conducted.

Statistical analysis was performed using SAS (Statistical Analysis System) software version 9.4 (SAS. Institute, Inc. Cary, North Carolina). Continuous variables are presented as mean ± SD, whereas categorical variables are presented as cases (n) and percentage rate (%). The sex-specific characteristics of the samples were obtained by simple tabulations and descriptive statistics.

3. Results and discussion

A total of 2203 patients with left and right IMT measurements constituted the source population (1205 from PLIC study and 998 from ESSE-RF study).

Table 1 summarizes the characteristics of the subjects recruited for the analysis. In both studies, there were more female (59.4% and 62.0% respectively in PLIC and ESSE-RF study) than male enrolled. ESSE-RF sample was younger (45.6 vs 53.9 years), more obese (26.6% vs 17.3%) and characterized by more smokers (24.8% vs 21.8%) than PLIC sample. On the other hand, individuals belonging to the PLIC study had higher mean values of systolic and diastolic pressure (131.5/82.5 vs 127.6/78.9 mm Hg).

Fig. 1 shows the prevalence of hypertension, high cholesterol and diabetes in the samples. Saint-Petersburg sample of ESSE-RF study had slightly more diabetic and hypertensive individuals, while the percentage of subjects with high cholesterol value was lower than in the other sample (67.1% vs 79.9%). This could be due, at least in part, to the enrollment setting of the studies: a lipid clinic for PLIC and a cardiology center for ESSE-RF. Given that, it is possible that some characteristics, such as diseases, are more prevalent.

As regards the lipid profile (HDL-C, LDL-C, TG) among individuals not treated with statins, there were no significant differences in lipid values between samples, except for the median LDL-C value, higher in the PLIC sample (p-value <0.0001, Fig. 2). However, the median LDL-C value was comparable among subjects receiving statin therapy (3.48 vs 3.45 respectively in PLIC and ESSE-RF study). On the other hand, the percentage of individuals with positive cardiovascular history was higher in ESSE-RF sample. This could also explain the higher mean value for IMT (0.71 ± 0.17 vs 0.63 ± 0.13) in the whole sample, and among patients without past cardiovascular events (regardless of statin treatment), despite some differences in major risk factors. Fig. 3 displays mean IMT at baseline for the samples analyzed. As can be seen, the red curve is shifted on the right, suggesting higher mean IMT values for Saint-

Table 1
Demographics and characteristics of subjects belonging to PLIC and ESSE-RF sample.

Characteristics	Milan			St.Petersburg		
	All n = 1205	Men n = 489, 40.6%	Women n = 716, 59.4%	All n = 998	Men n = 379, 38.0%	Women n = 619, 62.0%
Age, years	53 ± 9.4	52.8 ± 9.8	53.2 ± 9.1	45.6 ± 11.5	44.0 ± 11.6	46.6 ± 11.4
Height, m	1.63 ± 0.09	1.71 ± 0.07	1.58 ± 0.06	1.69 ± 0.10	1.78 ± 0.07	1.63 ± 0.06
Weight, kg	70.6 ± 12.9	78.3 ± 10.7	65.3 ± 11.5	77.8 ± 17.6	88.0 ± 15.3	71.6 ± 15.9
BMI, kg/m^2	26.4 ± 4.1	26.8 ± 3.2	26.2 ± 4.5	27.2 ± 5.3	27.8 ± 4.4	26.8 ± 5.8
BMI ≥30 kg/m^2, n (%)	208 (17.3%)	70 (14.3%)	138 (19.3%)	265 (26.6%)	103 (27.2%)	162 (26.2%)
Smoking status, n (%)	263 (21.8%)	130 (26.6%)	133 (18.6%)	247 (24.8%)	122 (32.2%)	125 (20.2%)
SBP, mm Hg	131.5 ± 16.6	134.7 ± 15.6	129.3 ± 16.9	127.6 ± 19.8	133.1 ± 18.3	124.2 ± 19.9
DBP, mm Hg	82.5 ± 9.1	84.3 ± 8.6	81.3 ± 9.3	78.9 ± 12.0	82.1 ± 11.9	77.0 ± 11.7
Prevalence of hypertension, n (%)	441 (36.6%)	193 (39.5%)	248 (34.6%)	388 (38.9%)	167 (44.1%)	221 (35.7%)
Total Cholesterol, mmol/L	5.7 ± 1.0	5.7 ± 1.0	5.7 ± 1.0	5.4 ± 1.2	5.4 ± 1.1	5.5 ± 1.2
Total Cholesterol > 4,9 mmol/L, n (%)	945 (78.4%)	379 (77.5%)	566 (79.1%)	653 (65.4%)	246 (64.9%)	407 (65.8%)
LDL-C, mmol/L	3.7 ± 1.0	3.8 ± 1.0	3.7 ± 0.9	3.5 ± 1.0	3.5 ± 1.0	3.4 ± 1.1
LDL-C>3,0 mmol/L, n (%)	922 (76.5%)	379 (77.5%)	543 (75.8%)	650 (65.1%)	264 (69.7%)	386 (62.4%)
HDL-C, mmol/L	1.4 ± 0.4	1.3 ± 0.3	1.5 ± 0.4	1.4 ± 0.4	1.2 ± 0.3	1.5 ± 0.4
HDL-C for men < 1,0 and for women < 1,2 mmol/L, n (%)	227 (18.8%)	90 (18.4%)	137 (19.1%)	254 (25.5%)	101 (26.7%)	153 (24.7%)
TG, mmol/L	1.2 ± 0.8	1.4 ± 1.0	1.1 ± 0.6	1.3 ± 0.8	1.5 ± 1.0	1.2 ± 0.7
TG > 1,7 mmol/L, n (%)	212 (17.6%)	126 (25.8%)	86 (12.0%)	206 (20.6%)	99 (26.1%)	107 (17.3%)
Prevalence of high cholesterol, n (%)	963 (79.9%)	397 (81.2%)	566 (79.1%)	670 (67.1%)	272 (71.8%)	398 (64.3%)
Glucose, mmol/L	5.0 ± 0.8	5.3 ± 0.8	4.9 ± 0.7	5.2 ± 1.0	5.4 ± 1.2	5.0 ± 0.8
Glucose 5,6-6,9 mmol/L, n (%)	155 (12.9%)	96 (19.6%)	59 (8.2%)	175 (17.5%)	92 (24.3%)	83 (13.4%)
Prevalence of diabetes mellitus, n (%)	34 (2.8%)	22 (4.5%)	12 (1.7%)	51 (5.1%)	25 (6.6%)	26 (4.2%)
ApoA, g/L	1.47 ± 0.2	1.38 ± 0.2	1.53 ± 0.3	1.59 ± 0.3	1.46 ± 0.3	1.66 ± 0.3
ApoB, g/L	1.13 ± 0.3	1.16 ± 0.3	1.12 ± 0.2	1.05 ± 0.3	1.08 ± 0.3	1.03 ± 0.3
Positive Cardiovascular history, n (%)	69 (5.7%)	42 (8.6%)	27 (3.8%)	293 (29.4%)	96 (25.3%)	197 (31.8%)
Mean IMT, left-side, mm	0.63 ± 0.2	0.66 ± 0.2	0.61 ± 0.1	0.72 ± 0.2	0.73 ± 0.2	0.71 ± 0.1
Mean IMT, left-side >0.9 mm, n (%)	70 (5.8%)	42 (8.6%)	28 (3.9%)	97 (9.7%)	44 (11.6%)	53 (8.6%)
Mean IMT, left-side >1.3 mm, n (%)	1 (0.1%)	1 (0.2%)	0 (0.0%)	4 (0.4%)	3 (0.8%)	1 (0.2%)
Mean IMT, right-side, mm	0.63 ± 0.1	0.64 ± 0.1	0.63 ± 0.1	0.71 ± 0.2	0.72 ± 0.2	0.71 ± 0.2
Mean IMT, right-side >0.9 mm, n (%)	47 (3.9%)	21 (4.3%)	26 (3.6%)	103 (10.3%)	47 (12.4%)	56 (9.1%)
Mean IMT, right-side >1.3 mm, n (%)	3 (0.3%)	0 (0.0%)	3 (0.4%)	5 (0.5%)	2 (0.5%)	3 (0.5%)

*BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, LDL-C – low density lipoproteins cholesterol, HDL-C – high density lipoproteins cholesterol, TG – triglycerides, ApoA – apolipoprotein A , ApoB – apolipoprotein B, IMT – intima-media thickness.

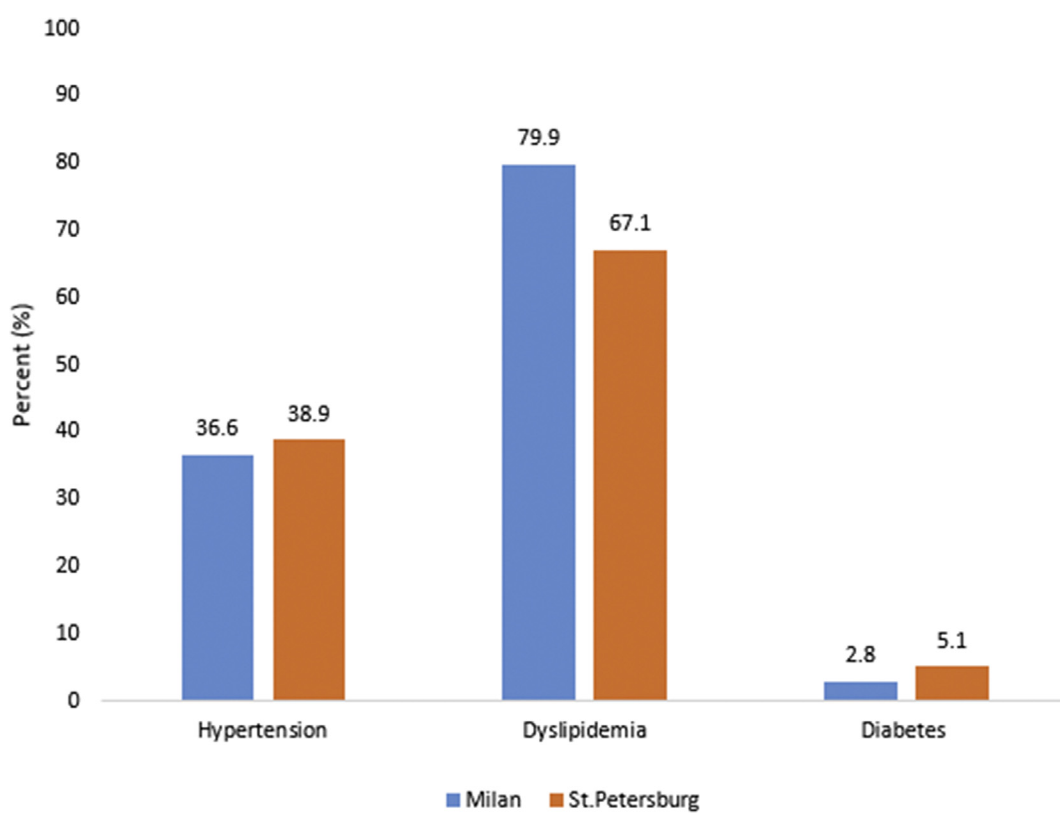


Fig. 1. Prevalence of hypertension, high cholesterol and diabetes in PLIC and ESSE-RF sample.

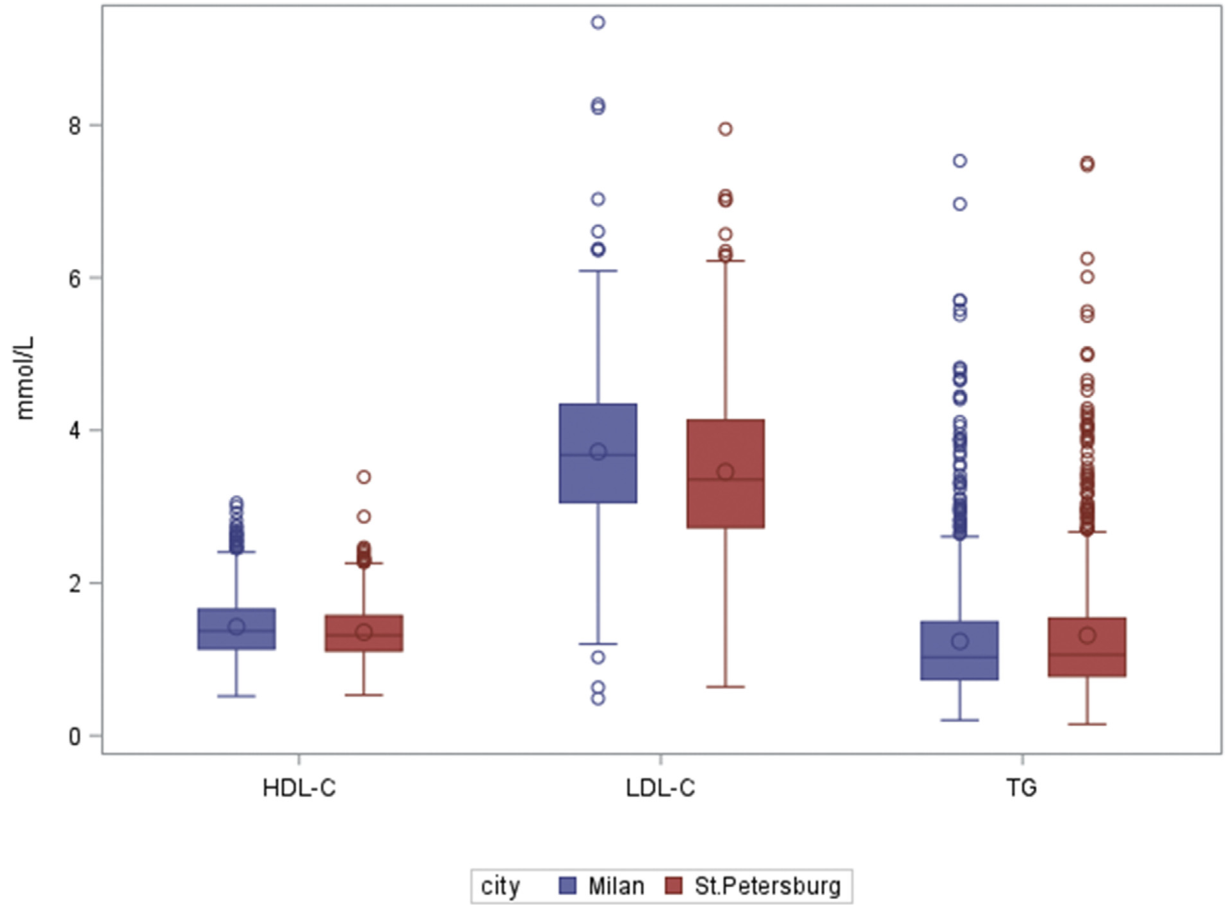


Fig. 2. Box plot of the lipid profiles for individuals not receiving statin therapy.

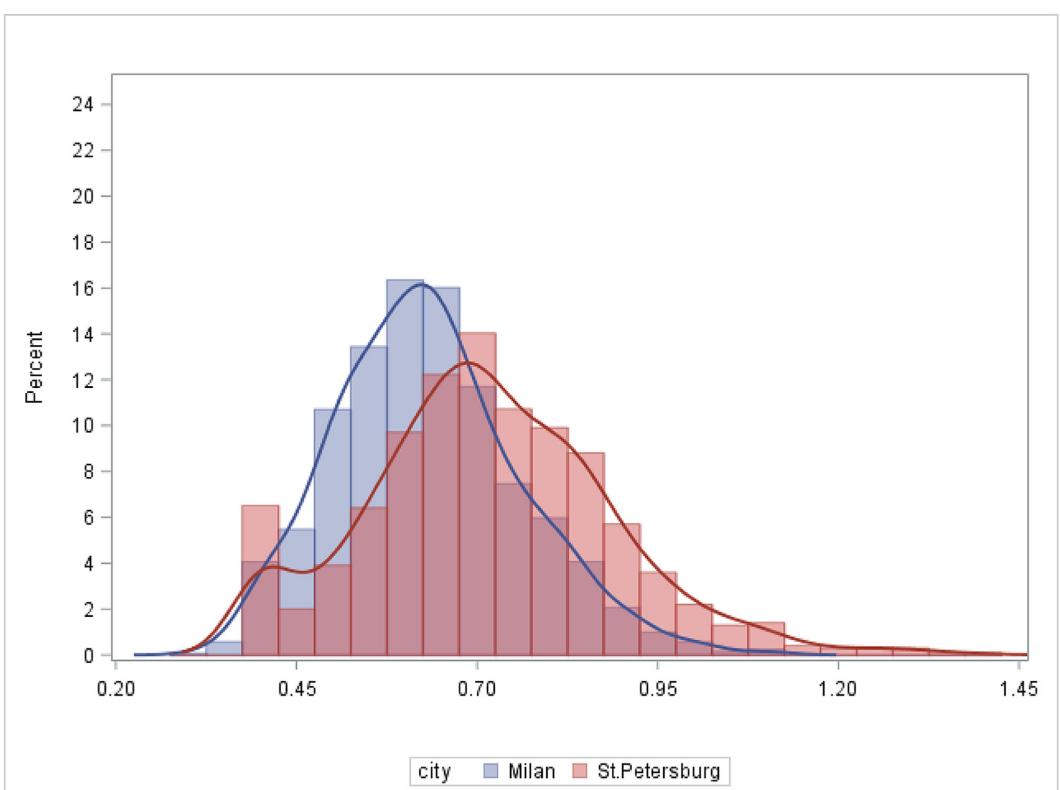
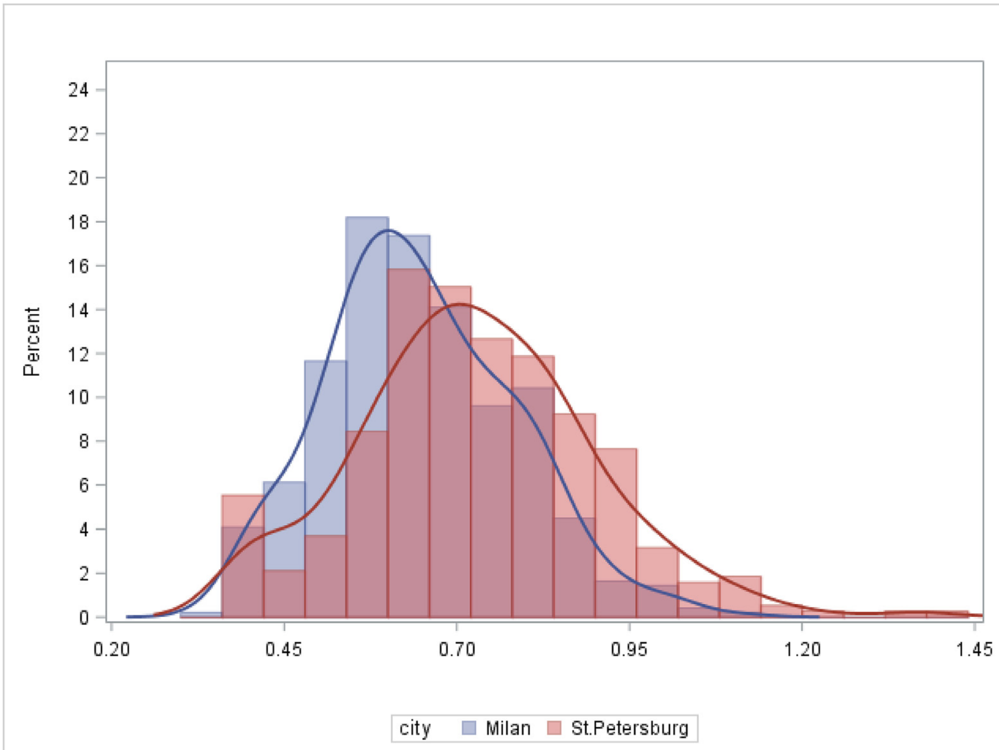


Fig. 3. Mean IMT distributions at baseline.

A



B

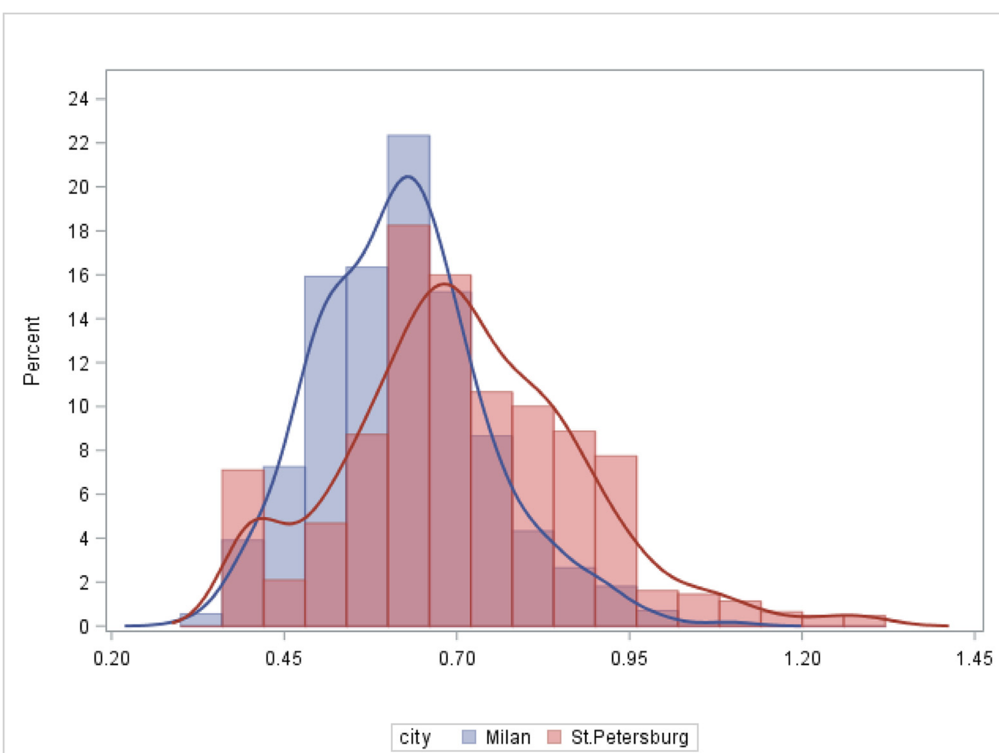
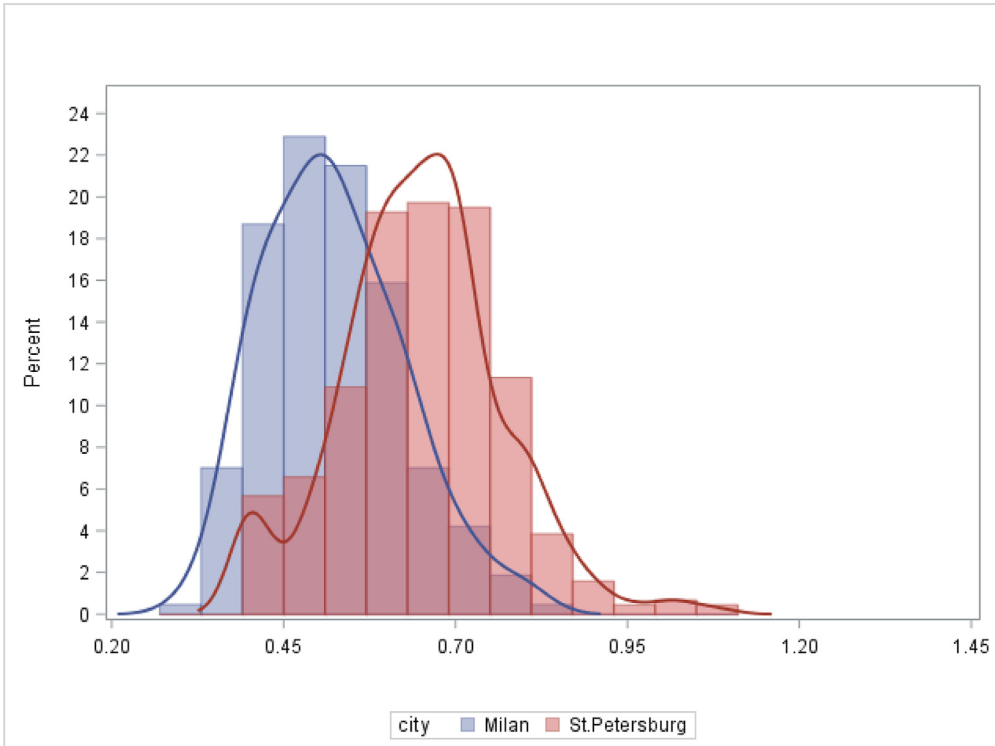


Fig. 4. Mean IMT distributions at baseline by men (A) and women (B).

A



B

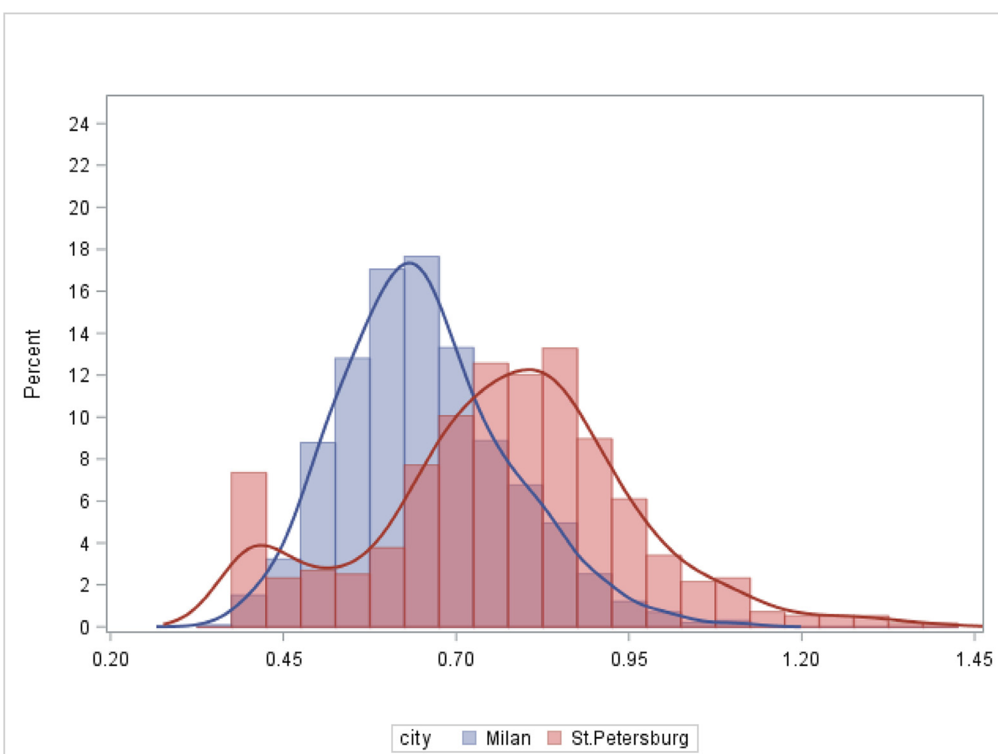


Fig. 5. Mean IMT distributions at baseline by subjects aged <45 (A) and aged >45 (B).

Petersburg sample of ESSE-RF study. This result was confirmed also by data on thickness (mean IMT>0.9) and plaque presence (mean IMT>1.3) both for left and right sides. Overall, the distributions remained the same also stratifying by gender (Fig. 4A and B). Generally, men showed greater mean IMT values than women for both sides (Table 1). This is consistent with prior literature. Finally, Fig. 5A and B illustrates mean IMT distributions at baseline by age (cut off 45 years old). The long right tail of the curves in Fig. 5B suggests that mean IMT increased with increasing patients' age, and this applies to both samples.

4. Conclusion

It has been demonstrated that, as far as these populations are culturally and geographically different, they are not so different based on characteristics analyzed. Integrating the study with an adequate follow-up, it could be interesting to look at the IMT patterns over time in these two samples, according to the prevalence of cardiovascular risk factors and to their modification in time.

Conflicts of interest

None declared.

Acknowledgments

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