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Research paper

Estimating 10-year cardiovascular disease risk in Asian patients with schizophrenia

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ABSTRACT

Objective: This study aims to describe the cardiovascular risk profile of Asian patients with schizophrenia.
Methods: Data was extracted from the databases of 139 patients with schizophrenia and 206 controls from two previous studies conducted at the Institute for Mental Health (IMH), Singapore. Their medical and smoking histories were obtained, and anthropometric parameters measured. Framingham risk score (FRS) calculator using body mass index was used to compute the 10-year cardiovascular disease risk (FRS_{BMI}) and the vascular age (VA_{BMI}) for each participant. Data on fasting lipids were available for 80 patients and all the controls; hence the FRS for lipids (FRS_{lipids}) and VA (VA_{lipids}) were also computed. The difference between VA and actual age was computed as VA_{diff}.
Results: The 10-year CVD risk and VA_{diff} based on lipids as well as BMI were significantly higher for patients compared to controls (all $p < 0.01$). There was a strong correlation between FRS_{lipids} and FRS_{BMI} ($r = 0.97$, $p < 0.001$). Significantly higher numbers of patients than controls were smokers and obese; and reported having dyslipidaemia.
Conclusions: We found a high risk of CVD in patients with schizophrenia as compared to controls; and conclude that patients with schizophrenia need regular physical health monitoring, especially for cardiovascular risk factors.

1. Introduction

Patients with schizophrenia have a reduced life expectancy of approximately 20 years below that of the general population, with cardiovascular diseases being one of the major causes for early mortality [1–4]. More than two-thirds of patients with schizophrenia die of coronary heart disease, as compared to one-half in the general population [1]. This high cardiovascular mortality is likely due to the high prevalence of metabolic disorders like obesity, hyperlipidaemia, insulin resistance, diabetes and hypertension in the population with schizophrenia [1,4]. Apart from the intake of antipsychotics [5,6], adverse lifestyle factors such as cigarette smoking, poor diet and sedentary behaviours [1,7,8] are known risk factors that contribute to the poor cardiovascular health in patients with schizophrenia. Furthermore, schizophrenia itself might be associated with higher cardiovascular risk, as suggested by studies that have reported that drug-naive patients with first episode psychosis have impaired fasting glucose tolerance, are more insulin resistant and have higher levels of plasma glucose, insulin, and cortisol than healthy controls [9–11].

The Framingham risk score (FRS) is a well-known gender-specific multivariable risk factor algorithm, which can be used in the clinical setting to estimate 10-year cardiovascular disease (CVD) risk and risk of individual CVD events (coronary, cerebrovascular, and peripheral arterial disease and heart failure) [12]. The Framingham heart study has helped to reduce the CVD mortality in developed countries by early identification of cardiovascular risk factors and the quantification of this risk using the FRS [13]. The FRS has been validated in several different populations [14–18], and more recently, in the mentally ill [19]. Ten-year CVD risk estimated using blood lipids (FRS_{lipids}) has been found to be significantly elevated in patients with schizophrenia as compared to healthy controls [20,21]. Although the Framingham study had developed a similar CVD risk calculator using the individual's body mass index (BMI, FRS_{BMI}) [12], we could not find any study which examined CVD risk using the BMI for patients with schizophrenia.

The CVD risk can be also presented as heart age or vascular age (VA) which refers to the age of the vascular system of an individual with different cardiovascular risk factors. The VA of an individual with certain cardiovascular risk factors is equivalent to the chronological age of a person with the same predicted risk but with all other risk factor levels in normal ranges (non-treated systolic blood pressure of 125 mm Hg, total cholesterol of 180 mg/dl, HDL of 45 mg/dl, non-smoker, non-

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diabetic) [12,22]. The VA was said to be a simpler concept for patients to understand [22].

There is a paucity of studies on CVD risk using the FRS and VA in Asian patients with schizophrenia. When coupled with a higher risk of CVD in Asia Pacific regions [23], this makes the identification and early intervention of CVD risk in patients with schizophrenia a clinically important area. It is also useful to examine the CVD risk using BMI in patients with schizophrenia, since BMI is more convenient to obtain than blood lipids in a clinical setting and there are no studies so far examining FRS_{BMI} in this population of patients. Here, we describe the cardiovascular risk profile of a sample of patients with schizophrenia and sought to examine the concordance between the FRS_{lipids} and FRS_{BMI}.

2. Materials and methods

2.1. Study setting and participants

Data was extracted from the databases from two previous studies conducted at the Institute for Mental Health (IMH), Singapore. Participants from these studies were previously recruited from the outpatient clinics at IMH. Eighty patients with schizophrenia were recruited from study 1 which was conducted from 2010 to 2011 [24]. Study 2 was an independent sample of 59 patients with schizophrenia and consisted of those who were screened for a randomized controlled trial from June 2009 and July 2011 [25]. Both the studies were reviewed and approved by the National Healthcare Group Domain Specific Review Board in Singapore. All participants provided written informed consent and were compensated for their time and inconvenience.

Current diagnosis of Schizophrenia was established using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders criteria (SCID I/P) [26]. Participants were excluded if they (i) were less than 30 years of age (since the FRS calculator is validated for individuals between the ages of 30 to 74) [12], (ii) had a current DSM-IV diagnosis of alcohol or other substance dependence (other than nicotine), or (iii) had a history of significant head injury/trauma. Data for controls was derived from study 1. Controls were recruited from the community by referrals, and had no history of psychiatric disorders as confirmed by the SCID, N/P [26].

2.2. Participant assessments

Demographic information and smoking history from all participants were collected. Medical histories of participants collected included history of dyslipidaemia, hypertension and diabetes mellitus. Details of current medications were also recorded. Total daily chlorpromazine (CPZ) equivalents were derived based on dose equivalence coefficients for typical [27,28] and atypical [28,29] antipsychotics. All information was obtained from both self-report and from available case records. Height and weight were measured and body mass index (BMI) computed. WHO BMI cut-off points were used to categorize BMI and define obesity in our sample [30]. Waist circumference (WC) was measured with participants standing, at the mid-point between the lower margin of the last palpable rib and the top of the iliac crest. Central obesity was defined using Asian cut-offs by the International Diabetes Federation criteria, which is >90 cm in males, and >80 cm in females [31]. Blood pressure was measured using an automated scale with the participant seated to the nearest 1 mm Hg. Eighty of the patients and all the controls provided a sample of fasting venous blood. Total cholesterol and high-density lipoprotein cholesterol (HDL-C) from the serum content were measured with analyzer LX-20PRO (Beckman Coulter, Germany).

2.3. Framingham risk and vascular age calculations

In this study, we computed the FRS using BMI for all the participants, and lipids for the patients and controls who had provided a fasted blood sample using the publicly available calculator. The FRS and VA based on BMI were calculated by including the following variables directly into gender-specific Cox regression models: Age, systolic blood pressure (SBP), treatment for hypertension, cigarette smoking, diabetes and BMI [12]. Cox models for FRS and VA based on lipids used total cholesterol (CHOL) and HDL cholesterol (HDL-C) instead of BMI. Participants were further categorized into those having low (<10%), intermediate (10–20%) and high (>20%) 10-year risk of CVD. The difference between VA and actual age of each individual (VA_{diff}_lipids, VA_{diff}_BMI) was calculated.

2.4. Statistical analysis

All statistical tests were performed on SPSS 23.0. Descriptive analyses were performed to describe the socio-demographic and metabolic profile of the study population. Data for SBP, chlorpromazine (CPZ) equivalents, FRS, VA and VA_{diff} was non-normal and therefore, we have reported the median and interquartile range (IQR) for these variables. Categorical variables were compared using chi-squared test. *t*-Test was used to compare age and BMI between patients and controls; whereas Mann Whitney U test was used for SBP, FRS, VA and $VA_{diff.}$ Significantly different variables between the patients and the controls were further analysed using multiple regression models with gender as covariate. Spearman correlation was used to examine the relation between the FRS and VA_{diff} based on BMI and lipids; and between FRS and CPZ equivalents. Kruskal-Wallis test was conducted to examine differences in FRS among the patients on typical, atypical and both antipsychotics, followed up by Mann Whitney *U* tests to evaluate pairwise differences among the three groups. Statistical significance was established at $p < 0.05$.

3. Results

A total of 139 patients and 206 controls were included in this study. Table 1 shows the demographic characteristics of the study sample. Chinese was the most common ethnic group followed by the Indians and Malays. A significantly higher number of patients were smokers, even after controlling for gender (OR = 4.81, CI: 2.60 to 8.91, $p < 0.001$).

The mean BMI of patients was 26.6 ± 5.2 kg/m^2, and was significantly higher than that of controls (24.4 ± 4.6 kg/m^2; $t = 4.03$, $p < 0.001$). One-fourth of the patients were obese and two-thirds had central obesity. Dyslipidaemia was the most commonly reported metabolic disorder for both the patients and controls. Most of the patients were prescribed a combination of typical and atypical antipsychotics (see Table 2). Nine patients were on anti-diabetic medications whereas one

Table 1
Demographic characteristics of patients and controls.

	Patients	Controls	p[a]
	n = 139	n = 206	
Age in years, mean (SD)	39.7 (5.6)	39.1 (6.2)	p = 0.383
Gender			p = 0.018
Male, n (%)	92 (66.2)	110 (53.4)	
Female, n (%)	47 (33.8)	96 (46.6)	
Ethnicity			p = 0.971
Chinese, n (%)	115 (82.7)	169 (82)	
Malay, n (%)	11 (7.9)	17 (8.3)	
Indian, n (%)	11 (7.9)	18 (8.7)	
Others, n (%)	2 (1.4)	2 (1.0)	
Current smokers, n (%)	46 (33.1)	18 (8.7)	p < 0.001
Male, n (%)	43 (46.7)	12 (10.9)	
Female, n (%)	3 (6.4)	6 (6.3)	
Marital status			p < 0.001
Single, n (%)	112 (80.6)	61 (29.6)	
Married, n (%)	16 (11.5)	124 (60.2)	
Widowed, n (%)	0 (0)	1 (0.5)	
Divorced/separated, n (%)	11 (7.9)	20 (9.7)	

[a] Chi-squared test was used to compare all the variables between patients and controls; except age, for which paired *t*-test was used.