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Cardiovascular risk in a first-episode psychosis sample: A 'critical period' for prevention?

Vivek H. Phutane, Cenk Tek, Lydia Chwastiak, Joseph C Ratliff, Banu Ozyuksel, Scott W. Woods, Vinod H. Srihari *

Yale University School of Medicine, United States

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ABSTRACT

Objective: Studies in first episode psychosis samples about status of cardiovascular risk factors have shown discordant results. We aimed to determine the 10-year risk of developing coronary heart disease in a sample of first episode psychosis patients referred to an early intervention clinic and compared the same with age, gender, and race matched controls from the U.S. National Health and Nutrition Examination Survey (NHANES).

Method: We conducted a cross-sectional analysis of baseline data of 56 subjects enrolled in first episode psychosis clinic from April 2006 to January 2010. This sample was compared with age, gender, and race matched 145 individuals drawn from NHANES 2005–2006 database. Sociodemographic and clinical variables were collected. Physical examination including laboratory evaluation was used to screen for common medical illnesses. The 10-year risk of developing coronary heart disease was calculated by using a tool developed by the National Cholesterol Education Program (NCEP-ATP III).

Results: There were elevated rates of smoking (46%) and hypertension (11%) albeit statistically significant differences from the control could not be demonstrated for these measures or weight, body mass index, or total or HDL cholesterol, fasting plasma glucose, status of diabetes and impaired fasting plasma glucose, HbA1C level. The 10-year median (range) risk of developing coronary heart disease in patients and controls was 1 (0–5)% and 0 (0–9)% respectively. The difference was not statistically significant.

Conclusions: First episode psychosis patients do not present with significantly higher cardiovascular risk than age and race-matched controls despite clinically significant prevalence of individual risk factors. This sample presents an opportunity for early intervention for the primary prevention of cardiovascular morbidity and mortality.

1. Introduction

Individuals with serious mental illness (SMI) die, on average, 25 years earlier than their peers (Colton and Manderscheid, 2006; Parks et al., 2006). While 30–40% of this premature mortality is attributable to suicide and accidental injury, cardiovascular disease accounts for the majority of early death. The single most common cause of death in patients with schizophrenia is cardiovascular disease (Osby et al., 2000; Capasso et al., 2008; Tiihonen et al., 2009). Patients with schizophrenia, relative to peers without SMI, experience a 3-fold increase in cardiovascular mortality between the ages of 18 and 49 and almost a 2-fold increase in mortality between the ages of 50 and 75 years (Osborn et al., 2007). They have a greater incidence of myocardial infarction than demographically similar persons without schizophrenia (Brown et al., 2000; Enger et al., 2004).

The causes of this increased cardiovascular burden in patients with schizophrenia are likely multi-factorial. Modifiable risk factors for cardiovascular disease include smoking, obesity, diabetes, dyslipidemia, and hypertension (Yusuf et al., 2004). When compared to age- and gender-matched controls, persons with chronic psychosis have higher rates of nicotine dependence (70–80% vs 25–30%) (de Leon and Diaz, 2005), obesity (45–55% vs 31–39%) (De Hert et al., 2009; Meigs et al., 2003), diabetes (13% vs 3%) (Goff et al., 2005), dyslipidemia (25–69% vs 24–48%) (De Hert et al., 2009; Meigs et al., 2003) and hypertension (27% vs 17%) (Goff et al., 2005). The largest study comparing cardiovascular risk factors in chronic schizophrenia patients, drawn from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Schizophrenia Trial, with age-, gender-, and race-matched controls from the U.S. National Health and Nutrition Examination Survey (NHANES) showed that patients had significantly higher 10-year coronary heart disease risk. This was due to higher rates of smoking, diabetes, and hypertension. Also, the mean (SD) duration of antipsychotic use in the CATIE study was 14.4 (10.7) years (Lieberman et al., 2005) and long-term use of antipsychotic

* Corresponding author. Tel.: +1 (203) 974 7816; fax: +1 (203) 974 7322.
E-mail address: vinod.srihari@yale.edu (V.H. Srihari).

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medications may play an important role in the increased risk for cardiovascular diseases (Goff et al., 2005; Newcomer, 2009). Antipsychotic medication use is associated with significant weight gain, dyslipidemia, and insulin resistance (Stahl et al., 2009).

In contrast to the consistent evidence across all measures of cardiovascular risk in chronic schizophrenia, studies of 'first episode' psychosis samples have been inconsistent. The first study comparing cardiovascular risk factors in drug-naïve first-episode schizophrenia patients with matched controls found that patients had significantly higher fasting plasma glucose levels. HDL cholesterol was not different, but total cholesterol was lower in patients (Ryan et al., 2003). These authors were unable to replicate these findings with a different sample, and, in a second study, reported that first-episode schizophrenia patients, their first degree relatives, and matched controls did not differ with respect to fasting plasma glucose levels (Spelman et al., 2007). Another study of drug-naïve first-episode psychosis patients compared to age, gender, and race matched controls showed that patients had a significantly higher prevalence of diabetes but lower frequencies of obesity and total and LDL cholesterol (Verma et al., 2009). A study of 38 first-episode psychosis patients compared to age, gender, and race matched controls did not find significant differences in fasting plasma glucose levels, glucose tolerance, body mass index, waist circumference and pulse pressure (Sengupta et al., 2008). Another study of antipsychotic-naïve, first-episode schizophrenia patients compared to healthy controls did not show significant differences in fasting glucose and insulin resistance (Arranz et al., 2004).

The use of specialized early intervention services (EI) to reduce long term psychosocial morbidity in psychotic disorders has been substantiated by several high quality studies (Marshall and Rathbone, 2006). The traditional focus of EI has been to deliver best available treatments during a putative 'critical period' for psychosocial development wherein intensive early intervention is hypothesized to achieve disproportionately positive results on long term outcomes. We propose an analogous formulation for reducing cardiovascular morbidity and mortality. The existence of EI clinics around the world, which are redefining care for early psychosis patients, presents an opportunity for the study and development of primary and secondary preventions of cardiovascular disease in schizophrenia.

Given the discrepancies in the reported prevalence of cardiovascular risk factors in early psychosis samples, the current study aimed to measure these risks again in a carefully characterized sample of patients referred to an early intervention clinic. Also, we used the best available risk calculator to formulate a 10 year risk estimate of developing coronary heart disease. We report a cross sectional comparison of these first-episode psychosis patients with age, gender, and race matched controls from the U. S. National Health and Nutrition Examination Survey (NHANES) (Centers for Disease Control and Prevention, 2005–2006).

2. Methods

Subjects for this analysis were drawn from an ongoing NIH-funded pragmatic randomized controlled trial titled Specialized Treatment Early in Psychosis (STEP). The broader goals of this trial are to determine the effectiveness and costs of a package of empirically supported treatments delivered within a U.S. community mental health center (Srihari et al., 2009). The subjects were consecutively enrolled in the study. The target sample of the NIH trial includes Connecticut residents between the ages 16 and 45 years, who are in the first five years since psychosis onset and willing to travel to New Haven for care. Subjects with co-morbid mental retardation or clear substance-induced psychosis are excluded from trial participation, but those with diagnostic uncertainty with respect to affective, substance-induced or medical etiologies are enrolled until these can be clarified over longitudinal follow-up.

We conducted a cross-sectional analysis of baseline data from 56 subjects enrolled in the trial between April 2006 and January 2010. Of 85 total enrollees in this period, 29 were not included, either because a complete profile of laboratory results was not yet available (n = 21), or because they were diagnosed with non-schizophrenia spectrum disorders by 6 months follow-up (n = 8). The 29 patients excluded from this analysis did not differ from those included with respect to demographic and clinical variables. We conducted a comparison of 56 trial subjects with 145 individuals drawn from the U.S. National Health and Nutrition Examination Survey (NHANES) (2005–2006) database. This is a probability sample of the civilian, non-institutionalized U.S. population and was designed to assess nutrition and health status of children and adults in the United States. The strength of this survey was the use of a combination of detailed interviews and physical examinations (Centers for Disease Control and Prevention, 2005–2006). Along with medical morbidities, it also screens for the presence of anxiety, depression, eating disorders, and panic disorders. Although the survey does not screen for psychotic disorder, it does query for the use of any psychotropic medications. The controls for this analysis neither had psychiatric morbidities nor were on any psychotropic medications. We matched each STEP patient with respect to age, gender, and race with all available controls from the NHANES 2005–2006 database.

Socio-demographic data was collected with a semi-structured questionnaire. Structured Clinical Interview for DSM-IV Axis-I disorders—Patient Edition was used for the assessment of the diagnosis (First et al., 1995). Nicotine use was assessed with AUS/DUS scale (Mueser et al., 1995) and a structured medical history included questions about previous diagnoses of hypertension or diabetes, other medical illnesses and current medications. Physical examination including vital signs, and laboratory evaluation was used to screen for common medical illnesses. Patients were asked to return, when necessary, for fasting blood draws (>8 h post-prandial).

Patients were categorized as having diabetes in NHANES according to standard clinical criteria (American diabetes association, 2005) with one caveat detailed below. These criteria included symptomatic hyperglycemia with a random plasma glucose level of ≥200 mg/dl, or a previous diagnosis confirmed by current prescription of oral hypoglycemics or insulin. Additional ADA criteria includes the use of fasting plasma glucose levels (FPG ≥ 126 mg/dl) or an oral glucose tolerance test (2 h postload glucose of ≥200 mg/dl) which have to be confirmed by repeat testing on a different day, but in NHANES this repeat measurement was not required to classify patients as diabetic. This classification is thus referred to as NHANES-defined diabetes in Table 1. Patients were categorized as having impaired fasting glucose

Table 1
Comparison of cardiovascular risk factors between the two groups.

Variables	Step	NHANES
	Patients (n = 56)	Controls (n = 145)
Smokers[a]	26 (46%)	52 (36%)
Weight (kg)[b]	80.1 (14.2)	81.5 (23.3)
Body Mass Index (kg/m^2)[b]	25.8 (4.8)	26.5 (7.0)
Systolic blood pressure[b]	126.1 (13.5)	116.3 (10.5)
Diastolic blood pressure[b]	71.3 (11.6)	63.9 (10.6)
NHANES-defined diabetes[b]	0 (0%)	2 (1%)
Impaired fasting glucose (FPG: 100–125 mg/dl)[b]	9 (16%)	18 (12%)
Total Cholesterol, mg/dl[b]	171.8 (28.1)	164.4 (33.5)
HDL Cholesterol, mg/dl[b]	48.2 (11.3)	51.2 (12.9)
Prevalence of Metabolic Syndrome, n (%)	11 (19.6%)	24 (16.6%)
10-year risk for developing coronary heart disease, %[c]	1 (0–5)	0 (0–9)

[a] n (%).
[b] Mean (SD).
[c] Median (range).