



Coronary artery disease in adults with schizophrenia: Anatomy, treatment and outcomes



Ryan A. Todd^{a,1}, Adriane M. Lewin^{b,c,1}, Lauren C. Bresee^{d,e,1}, Danielle Southern^{b,1}, Doreen M. Rabi^{b,c,*,1}, on behalf of the APPROACH Investigators

^a Department of Psychiatry, University of Toronto, Canada

^b Institute of Public Health, University of Calgary, Canada

^c Department of Medicine, University of Calgary, Canada

^d Alberta Health Services, Canada

^e Department of Community Health Sciences, University of Calgary, Canada

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ABSTRACT

Background: People with schizophrenia are at significantly greater risk of cardiovascular disease-related mortality. We set out to determine if people with and without schizophrenia who undergo coronary artery catheterization differ with respect to coronary anatomy, coronary artery disease management, or outcome.

Methods and results: This study used provincial administrative data and a clinical registry that included all individuals who undergo coronary catheterization in Alberta, Canada. Individuals with schizophrenia were identified in hospital discharge data using ICD-9 codes. We identified 271 Albertans with a hospital discharge diagnosis of schizophrenia and a subsequent coronary catheterization and were matched with 1083 controls without schizophrenia that had undergone a coronary catheterization. Extent of coronary disease was assessed using 1) left ventricular ejection fraction; 2) the Duke Jeopardy Score (a valid measure of myocardium at risk for ischemic injury); and 3) a categorical assessment of coronary anatomy risk. People with schizophrenia were less likely to be categorized as high risk on the Duke coronary index ($p < .005$) and more likely to be categorized as having a normal coronary anatomy ($p < .05$). Significant differences in mortality were found among those with and without schizophrenia both before and after adjustment for clinical differences.

Conclusions: Our results suggest that people with schizophrenia have less severe coronary atherosclerosis, and are less likely to receive revascularization. Despite less severe coronary atherosclerosis, individuals with schizophrenia had a significantly higher mortality following catheterization. Interventions to increase therapeutic adherence and clinical follow up of patients with mental illness may improve health outcomes.

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1. Introduction

Schizophrenia is a potentially debilitating chronic mental illness that affects approximately 1% of the Canadian population [1]. Schizophrenia also confers significant risk for physical illness and premature mortality. Individuals with schizophrenia are known to have a 20% reduction in life expectancy and this increased mortality rate has been persistent over time despite major advances in psychiatric care [2].

Persons with schizophrenia are at increased risk for cardiovascular disease (CVD) – related mortality compared to those without schizophrenia [3,4]. This increase in risk has been attributed to a number of

factors including a higher burden of comorbid illness, a high prevalence of smoking and sedentary lifestyle, and the use of atypical antipsychotic agents (AAPs), a class of medications which are known to increase the risk of metabolic syndrome, obesity and type 2 diabetes [5–7].

It has been suggested that inequitable access to care may be another mediating mechanism underlying the association between schizophrenia and poor CVD outcomes [8]. Previous research has shown that people with schizophrenia are less likely to undergo cardiac catheterization, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG) relative to those without schizophrenia [9–12]. Factors such as cardiac surgeon selection bias [13], socio-economic barriers [14], and informed consent issues [6] have been postulated as possible causes for this discrepancy. However, to the best of our knowledge, the possibility of these treatment differences being related to underlying differences in the anatomy of coronary disease has not been explored. It is unclear whether this apparent discrepancy in treatment may be explained by differences in coronary anatomy, such that persons

* Corresponding author at: Assistant Professor, University of Calgary, TRW 3E21, 3280 Hospital Dr. NW, Calgary AB T2N 4N1, Canada. Tel.: +403 220 8867; fax: +403 210 8118. E-mail address: doreen.rabi@albertahealthservices.ca (D.M. Rabi).

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with schizophrenia have coronary disease that simply may not be amenable to revascularization.

The objectives of this study were to: 1) ascertain the proportion of people with and without schizophrenia who receive coronary revascularization (PCI or CABG) following cardiac catheterization; 2) describe the relationship between the clinical profiles and coronary anatomy of those with and without schizophrenia; and 3) determine mortality among persons with and without schizophrenia following coronary catheterization.

2. Methods

2.1. Study cohort and data sources

This cohort study was performed using administrative health and clinical registry data from the Alberta Health Services Discharge Abstract Database (DAD) from Alberta Health and Wellness, and the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) [15]. The DAD contains demographic and clinical information for all patients discharged from any hospital using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and ICD-10-Canada (ICD-10_CA). APPROACH is an ongoing prospective data collection initiative that has captured detailed clinical information on all patients undergoing cardiac catheterization and subsequent interventions in the province of Alberta, Canada since 1995 [6]. After data collection from the APPROACH database, a data enhancement process verifies patient comorbidities and maximizes data completeness [7,8]. Lastly, we obtained information on mortality for all patients through quarterly linkage to the Alberta Bureau of Vital Statistics. Individuals in these datasets are linked using a unique lifetime identifier, the Personal Health Number (PHN).

2.2. Identification of study cohort

People with schizophrenia (cases) were identified using the DAD. Those who had a hospital discharge between March 14, 1995 and December 31, 2009 with a diagnosis of schizophrenia (ICD-9 295; ICD-10 F20) in any diagnostic field were classified as having schizophrenia [16]. These people were then cross-referenced with the APPROACH registry to identify those who underwent coronary revascularization. They were then matched by age, sex, fiscal year, and indication for coronary catheterization in a ratio of 1 case to 4 controls with people in the APPROACH registry who had undergone coronary catheterization but without a prior discharge diagnosis of schizophrenia. Excluded from this study were people for whom the coronary catheterization preceded the first recorded hospital discharge of schizophrenia, non-Alberta residents, and people with incomplete comorbidity data.

2.3. Clinical and outcome variables

Using data from APPROACH, extent of coronary disease was assessed using 3 different measures: 1) left ventricular ejection fraction (LVEF); 2) the Duke Jeopardy Score, which encompasses both the percentage of stenosis in a coronary lesion and the volume of myocardium at risk (the Duke Jeopardy Score has been validated in the APPROACH population and has been shown to provide independent prognostic information in people with ischemic heart disease) [9,10]; and 3) a categorical assessment of coronary anatomy risk, with high risk anatomy defined as 3-vessel disease, left main disease, or 2-vessel disease involving the proximal left anterior descending coronary artery per the Duke Coronary Index.

2.3.1. Ethics approval

The Conjoint Health Research Ethics Boards of the University of Calgary approved this study.

3. Statistical methods

The baseline characteristics were compared using chi-square, Fisher's exact, or t-tests as appropriate. Treatment and revascularization within one year following catheterization were compared between groups using chi-square tests. Differences in survival were assessed using Kaplan–Meier curves and Cox proportional hazard models. After ensuring that the proportional hazard assumption was met, we evaluated survival using the corrected group prognosis method, adjusted for comorbidities, clinical characteristics and treatment [17]. We performed a sensitivity analysis limited to people whose indication for catheterization was acute myocardial infarction (AMI) (either ST-elevation or nonST-elevation MI). All analyses were performed using SAS software version 9.1 (SAS Institute Inc., Cary, NC, USA).

4. Results

We identified 271 people with a hospital discharge diagnosis of schizophrenia between March 14, 1995 and December 31, 2009 and a subsequent coronary catheterization. These individuals were matched with 1083 controls that had undergone a coronary catheterization but had no hospital discharge record of schizophrenia. Clinical and demographic profiles of those with and without schizophrenia are presented in Table 1. People with schizophrenia had a greater comorbid disease burden than people without schizophrenia. A greater proportion of people with schizophrenia than controls had cerebrovascular disease (8.9% vs. 5.4%, $p = 0.031$), pulmonary disease (23.3% vs. 13.6%, $p < 0.001$), congestive heart failure (21.4% vs. 13.4%, $p < 0.001$), renal disease (7% vs. 3.3%, $p = 0.006$) and diabetes (25.5% vs. 20.1% $p = 0.054$) at the time of catheterization. Additionally, a greater proportion of people with schizophrenia were smokers (48% vs. 35.1%, $p < 0.001$).

No significant differences were seen in cardiac event history, including prior MI (32.5% vs. 30.4% $p = 0.50$), prior PCI (3.7% vs. 4.2% $p = 0.73$), and prior CABG (1.9% vs. 2.8% $p = 0.35$).

Those with schizophrenia were less likely to have a LVEF, over 50% relative to those without schizophrenia (53.1% vs. 61.1%, $p = 0.021$), but were more likely to have an LVEF in the 20–34% class than those without schizophrenia (8.9% vs. 5.0% $p = 0.021$) (Table 2). These clinical differences were also found when the analysis was limited to those with AMI.

In addition, people with schizophrenia were less likely to be categorized as high risk on the Duke Coronary Index (18.8% vs. 25.6% $p = 0.021$) and more likely to be categorized as having a normal coronary anatomy (32.5% vs. 25.6% $p = 0.021$). When analysis was restricted to those with AMI, such differences in clinical anatomy were not seen. People presenting with AMI, irrespective of schizophrenia status, appeared to have similar coronary anatomy.

Within one year of catheterization, a greater proportion of people with schizophrenia were treated medically than those without schizophrenia (53.1% vs. 45.2% $p = 0.05$) (Table 3). Those with schizophrenia were treated less frequently with surgical interventions such as CABG (11.4% vs. 15.1% $p = 0.05$) and PCI (35.4% vs. 39.8% $p = 0.05$). These differences were attenuated but still persisted when the analysis was restricted to those with AMI.

Significant differences in mortality were found among those with and without schizophrenia both before (crude hazard ratio [HR]: 2.19; 95% CI 1.68–2.85; $p < 0.001$) and after adjustment for clinical differences (adjusted HR: 1.85; 95% CI 1.39–2.4; $p < 0.001$) (Table 4). Similarly, the Kaplan Meier curve (Fig. 1), which displays survival up to 15 years after catheterization shows a significant decrease in survival among those with schizophrenia. Cause of death data was available for 67 of the people in the cohort (4.9%). Among this small sub-sample of people, AMI was the most frequently reported cause of death and there were no significant differences in cause of death among those with or without schizophrenia (Fig. 2).

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