



Review

Cardiovascular diseases among patients with schizophrenia



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ABSTRACT

The presence of comorbid physical illnesses especially, cardiovascular diseases (CVD) in schizophrenia is a growing area of concern in recent years. In order to reduce disease burden, to improve quality of life and to provide holistic care, it is important to know about the relationship between schizophrenia and CVD. The objective of this review is to explore the extent of CVD problems, relevant risk factors and potential measures for early diagnosis and prevention of CVD among patients with schizophrenia. Worldwide studies show that patients with schizophrenia have a higher mortality and lower life expectancy than the general population. CVD is the leading cause of increased mortality in schizophrenia. Common CVD risk factors in schizophrenia include metabolic syndrome, sedentary behaviour, tobacco smoking, effects of antipsychotics, long chain omega-3 fatty acid deficiency and shared genetics between CVD and schizophrenia. The potential methods for early detection and prevention of CVD in schizophrenia are also discussed. Though the patients with schizophrenia form a high risk group for CVD, consensus guidelines for early detection and prevention of CVD in schizophrenia are lacking. Comorbidity of CVD in schizophrenia needs more serious attention by clinicians and researchers.

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Abbreviations: ABI, ankle brachial index; BP, blood pressure; BMI, body mass index; CATIE, clinical antipsychotic trials of intervention effectiveness; CIMT, carotid intima media thickness; CRF, cardio-respiratory fitness; CVD, cardiovascular diseases; DALY, disability-adjusted life year; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FGA, first generation antipsychotics; GBD, global burden of disease; GP, general population; GWAS, genome-wide association studies; HDL, high density lipoprotein; JBS, joint british societies score; LCn-3, long-chain omega-3; LDL, low density lipoprotein; MetS, metabolic syndrome; NCEP, national cholesterol education program; PCBs, polychlorinated biphenyls; PF, physical fitness; PGC, psychiatric GWAS consortium; RCT, randomized controlled trial; SGA, second generation antipsychotics; SMR, standardised mortality ratio; SZ, schizophrenia; YLD, years lived with disability; WHO, World Health Organization.

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1. Introduction

Schizophrenia is a chronic and debilitating mental illness which causes substantial degree of disability. About one out of 100 individuals will experience this mental illness in his lifetime, and this figure is similar around the world (Jablensky, 1995). The burden caused by schizophrenia is huge and multifaceted (Rössler et al., 2005). The Global Burden of Diseases (GBD) study showed that schizophrenia contributes significantly to the GBD, with 1.1% of total disability-adjusted life years (DALYs) and 2.8% of years lived with disability (YLDs) attributed to this (Murray and Lopez, 1997). In the World Health Report 2001, the 8th leading cause of DALYs worldwide in the age group 15–44 was schizophrenia (World Health Organization, 2001). Furthermore, people with schizophrenia are vulnerable to developing physical illnesses such as diabetes, metabolic syndrome, cardiovascular diseases (CVD), respiratory diseases and cancer (Brown et al., 2000). The physical comorbidities complicate their disabilities and increase the disease burden. Health care providers frequently pay more attention to the psychological and behavioural problems and ignore physical diseases such as CVD in schizophrenia and the patients have been shown to receive a lower standard of care after CVD is diagnosed (Druss et al., 2000). A cross-sectional study by Smith et al. reported a systematic under-recognition and under-treatment of CVD of patients with schizophrenia within primary care (Smith et al., 2013). The present overview has been planned to shed light on the issue of comorbidity of CVD among the patients with schizophrenia. The aim of this review is to point out the causes of mortality in schizophrenia, to discuss about the important risk factors of CVD in schizophrenia and to recommend the potential early diagnostic and preventive measures for CVD in schizophrenia. In this narrative review, we conducted PubMed, Scopus and Google search using the following combinations of keywords: 'Schizophrenia', 'Schizophrenic disorder', 'Cardiovascular diseases', 'Coronary disease', 'vascular disease', 'Risk factors', 'mortality', 'death', and 'prevention'.

2. Mortality and life expectancy in schizophrenia

Schizophrenia has been associated with increased risk of several adverse outcomes which lead to a reduced life expectancy. A meta-analysis which extracted data from 37 studies in 25 countries, showed that the risk of death of people with schizophrenia was 2.5 times the general population (Saha et al., 2007). An earlier meta-analysis also reported significantly increased mortality rate in people with schizophrenia (Brown, 1997). A retrospective study of mortality among 3623 patients with schizophrenia in Alberta, Canada found that the risk of mortality in schizophrenia patient was approximately double that of the Alberta population (Newman and Bland, 1991). Another life expectancy study on large samples in Nordic countries (Denmark, Sweden and Finland) reported that the overall mortality was 2 to 3 times higher than the general population (Laursen et al., 2013).

It was observed that life expectancy of people with schizophrenia is shorter than that of the general population and standardised mortality ratio (SMR) is high. Among persons with bipolar disorder or schizophrenia in Nordic countries, life expectancy has been shown to be 12 to 20 years shorter in men and 11 to 17 years shorter in women, compared to the general population (Laursen et al., 2013). In Alberta, Canada, schizophrenia patient have approximately 20% shorter life expectancy than that of the general population (Newman and Bland, 1991). A 11-year follow-up study in Finland (FIN11 study) showed that the gap in life expectancy between patients with schizophrenia and the general population had not significantly changed over time, for example, the gap was 25 years in 1996 and in 2006, it was 22.5 years (Tiihonen et al., 2009). We can summarize that people with schizophrenia have a higher mortality rate and about 2 to 3 times greater risk of death than the general population. Also, their life expectancy is around 15–20 years shorter than the general population.

2.1. Causes of mortality in schizophrenia

The significantly lower life expectancy in schizophrenia can be attributed to death from both natural and unnatural causes. Causes of natural deaths in schizophrenia include cardiovascular diseases, respiratory diseases, cancer, unrecognized medical diseases, poor compliance, refusal of treatment for medical diseases, unhealthy life style, substance misuse and antipsychotic drug side effects (Brown et al., 2000; Bushe et al., 2010; von Hausswolff-Juhlin et al., 2009). Unnatural deaths are mainly caused by suicides and accidents (Brown, 1997). Natural and unnatural causes account for about 60% and 40% of all deaths in schizophrenia respectively (Ringen et al., 2014).

The contribution of cancer to mortality in schizophrenia ranges from 7 to 21% of all causes of deaths (Brown et al., 2000; Capasso et al., 2008; Chong et al., 2009; Dean and Thuras, 2009; Fors et al., 2007; Mortensen and Juel, 1993; Tran et al., 2009). The cancer mortality rate among patients with schizophrenia has been reported higher than the general population in studies in Australia and Denmark (Dalton et al., 2008; Lawrence et al., 2000). Lung and breast cancer are the two commonest malignancies in schizophrenia (Bushe et al., 2009; Catts et al., 2008; Hippisley-Cox et al., 2007). An 11-year prospective mortality study among 3470 patients with schizophrenia revealed that lung cancer contributed 50% of all cancer in males and breast cancer contributed 39% of all cancer in females (Tran et al., 2009). 80% of incident cases of breast cancer arose among patients with schizophrenia who were over 50 years old (Bushe et al., 2009). A remarkably large mortality study among 17,600 patients with schizophrenia over seven years period reported mortality rate ratio for CVD 2.07 and 1.72 and malignant neoplasms 1.24 and 1.32, for males and females, respectively (Laursen et al., 2007).

The contribution of respiratory diseases and other natural causes to mortality in schizophrenia varies across the studies. There may be different causes of excess mortality in Asian

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