



The risk for a first acute coronary syndrome in patients treated with different types of antidepressants: A population based nested case-control study☆

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ABSTRACT

Background: Tricyclic antidepressants (TCAs) are still used in 30% of anxiety/depression cases and have been related to increased cardiovascular risk. Newer serotonin/norepinephrine reuptake inhibitors (SSRIs/SNRI_s) safety remains conflicting. Our aim was to assess the risk of a first acute coronary syndrome (ACS) in patients treated by various types of antidepressants.

Methods: Study was a retrospective nested case-control of 40–80 years old northern-Israeli members of Clalit Health Services (CHS) during 1.1.2003–31.12.2013. Patients with severe psychiatric, cardiac or systemic diseases, or pre-enrollment antidepressants were excluded. Cases that had a first ACS during the study period were matched in 1:30 ratio with controls. The association between antidepressants use and ACS was tested by adjusted multivariable conditional logistic regression.

Results: The cohort included 535,315 individuals 128,550 of whom met the exclusion/inclusion criteria. 3391 Cases with first ACS, (incidence rate of 24.6/10,000 person years) were matched with 88,016 controls.

ACS was not associated with use of either SSRIs/SNRI_s or TCA_s compared with no antidepressants use. However, treatment by SSRIs/SNRI_s was associated with a 36% decreased risk ACS compared to TCA_s, OR = 0.64, 95%CI (0.43–0.95), $p = 0.029$. Age 40–64 years, male gender and metabolic syndrome associated with reduced risk of ACS among SSRIs/SNRI_s compared to TCA_s users.

Conclusion: In this study of patients without prior cardiovascular disease—neither antidepressant group imposed excess risk for ACS, compared to no treatment. SSRIs treatment seemed safer compared to TCAs in regard of ACS. This study probably adds to our confidence of preferring SSRIs over TCAs in patients without prior cardiovascular disease.

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1. Background

Cardiovascular diseases and mental depression are leading health problems worldwide [1,2]. Nearly half of healthy men and a third of women will have coronary artery disease after the age of 40 years, and the lifetime risk of major depression was shown to be 16.2% [2]. The two conditions interrelate. It has been reported that one out five patients with coronary artery disease (CAD) and a third of patients with

congestive heart failure may demonstrate varying levels of depression [3,4]. Depression is a recognized risk factor for acute coronary events in healthy people and CAD patients [5].

Anxiety and depressive disorders have increased in prevalence causing a parallel increase in antidepressant therapy utilization [6–8], rising from 2.6% in 1986 to 7.1% in 2000 in the USA [8]. Tricyclic antidepressants (TCAs) are the most archaic type of therapy and still used in 30% of cases. They were reported to be related to increased risk cardiovascular events [9]. Newer drugs include selective serotonin reuptake inhibitors (SSRIs), used in 50% of cases, serotonin norepinephrine reuptake inhibitors (SNRIs), used in 14%, and others used in the rest of the patients [9]. There are conflicting data regarding the effect of SSRIs on cardiovascular disease risk [9–12]. Thus it is largely unknown whether SSRIs protect, or increase the risk cardiovascular events. The cardiovascular safety profile of SNRIs has not been established yet.

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The aim of this study was to assess the effects of treatment with antidepressants on the incidence of a first acute coronary syndrome (ACS) and specifically to compare SSRIs to other antidepressant treatment groups for the same outcomes.

2. Methods

2.1. Database and study design

The study was designed as a retrospective nested case control study based on the Clalit Health Services (CHS) clinical database. CHS is the largest health maintenance organization in Israel, providing medical care to more than one-half of the Israeli population [13]. The computerized database was established in 1998 and includes data from primary and specialist community care providers, hospital admissions, laboratory test results and pharmacies. Chronic diseases are coded according to the international

classification of disease 9th revision (ICD9) and the International Classification of Primary Care (ICPC). Dispensed prescriptions of medications are coded according to the Anatomic-Therapeutic-Chemical (ATC) index. The database also includes demographic variables based on the national Israeli population registry and anthropometric and lifestyle variables such as body mass index and smoking based on the documentation from primary care clinic visits. Updated mortality information is available from the national population registry.

2.2. Patient selection

The study was based on a retrospective cohort of (CHS) members in the Haifa-Western Galilee and North Districts population. Fig. 1 provides a description of the cohort.

Patients were included if they were CHS members aged 40–80 years in –1.1.2003, and remained a member until 31.12.2013.

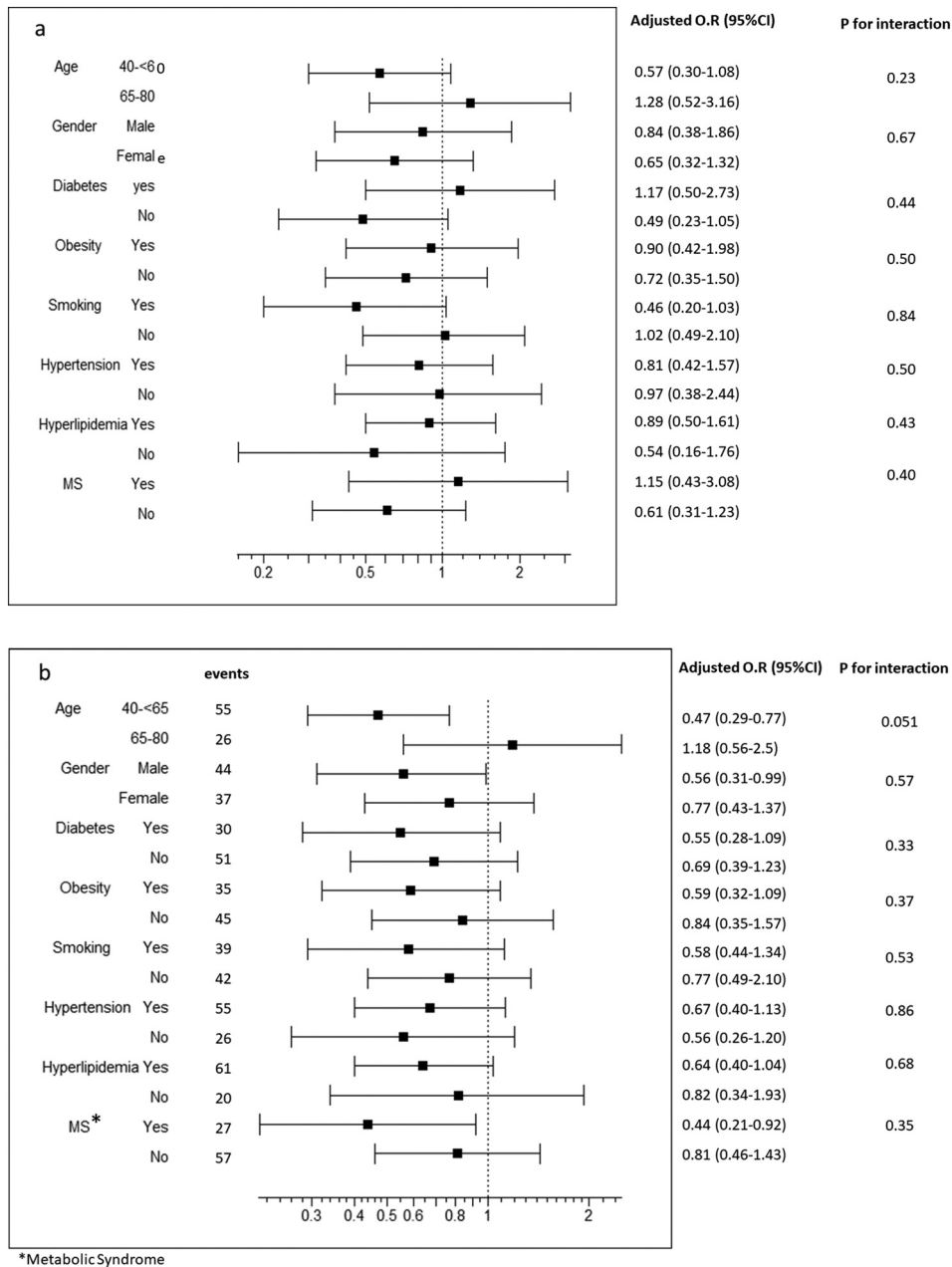


Fig. 1. Forest plots for SSRIs use and the risk for an acute coronary syndrome (ACS) a: SSRI or SNRI use association with ACS, compared with no-Antidepressants use, stratified by risk factors b: SSRI or SNRI use association with ACS, compared with TCA use, stratified by risk factors.

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