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Emotional distress as a predictor of statin non-adherence among Swedish first-time myocardial infarction patients, 2006–2013

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ABSTRACT

Background: Emotional distress (depression and anxiety) has been known to affect mortality after a myocardial infarction (MI). One possible mechanism is through medication non-adherence. Few studies have investigated the link between statin adherence and emotional distress, and results are not consistent. We aimed to explore whether emotional distress affects adherence among first-time MI patients younger than 75 years old receiving a prescription for the first time.

Methods: We identified first-MI individuals younger than 75 years from the SWEDEHEART national quality registers discharged with a statin prescription. The main exposure was the anxiety/depression portion of the EQ-5D from Interview 1 (6–10 weeks post-MI) and Interview 2 (12–14 months post-MI). We calculated adherence from the Swedish Prescribed Drugs Register during three observation periods (OP): [1] Interview 1 to Interview 2, [2] one year post Interview 2, and [3] two years post Interview 1.

Results: Emotional distress at Interview 1 was not associated with statin adherence for OP1 (RR: 0.99, 95% CI: 0.98, 1.01). Emotional distress at Interview 2 was associated with lower adherence one year later (RR: 0.95, 95% CI: 0.93, 0.98). Emotional distress at Interview 1 was associated with a small decrease in adherence in the complete OP for adherence (RR: 0.98, 95% CI: 0.96, 0.99).

Conclusion: Emotional distress was marginally, but independently, associated with lower adherence to statin two years after the MI. Our study suggests that emotional distress may be an important factor for long-term statin adherence, and, thus, may play a clinically important role in long-term outcome.

1. Background

Depression and anxiety have both been identified as risk factors for cardiovascular disease. Although the two have different presentations, studies have found an increased prevalence of both in patients who survive a myocardial infarction (MI). In MI survivors, the prevalence of depressive symptoms has been estimated to be approximately 30%, and 20% for major depression as of 2006, though current prevalence is uncertain [1]. There was a similarly high prevalence of anxiety reported in patients with MI, ranging from 30 to 40% [2]. Depression is associated with 50% increased risk of new cardiac events, a doubling in the risk of all-cause mortality, and almost three times increased risk of cardiac mortality [3]. Anxiety has also shown significant association with MI prognosis, with a 36% increased risk of adverse cardiac outcomes [2]. Less is known of the mechanisms by which this type of emotional distress, i.e. depression and anxiety, can affect prognosis, but one hypothesis is that those with emotional distress may be less likely to adhere to evidence-based medication regimens.

There have been several studies on the association between emotional distress and adherence, with most focusing on the entire medication regimen in patients with stable coronary artery disease or in those who have recently suffered an MI. Despite somewhat varied methodology, the results are consistent, generally showing that individuals with depression or anxiety are more likely to not adhere to cardiac medications than those without [4–10]. These studies, however, have not evaluated whether emotional distress affects usage separately depending on type of medication. Different medication may have different side effects, which can affect how emotional distress impacts its adherence.

Statins are prescribed to a majority of MI patients as part of their long-term secondary prevention regimen, and are considered one of the key medications necessary to improve survival and prevent reinfarction. Appropriate adherence to this class of medication has been shown to have the potential for decreasing mortality after an MI by up to 25%

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[11]. However, in part because of a myriad of criticism, both online and among social circles, statins have been shown to suffer from poor adherence rates, reported to be as low as 30% one year later [12]. Because of its importance, statin use is a key area of secondary prevention that may be affected by emotional distress. Few studies investigate this [13–16]. So far all have focused on depression, and results have been conflicting, with significant associations with non-adherence present in three studies, and one showing no association. There is limited data regarding statin adherence in post-MI patients, and what exists is often limited in generalizability. The comprehensive SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) quality registers provide a unique opportunity to investigate emotional distress in first-time MI patients.

The primary objective of the present study is to determine whether symptoms of emotional distress, assessed both after the MI and one year later, affect short- and long-term adherence to statins first prescribed after a first MI among patients aged 74 years old and younger from SWEDEHEART registers. Our secondary goal was to investigate the association between severe emotional distress and diagnosed clinical depression and/or anxiety with statin adherence.

2. Methods

2.1. Data sources

Data were obtained from the SWEDEHEART collection of national quality registers for cardiovascular disease, which includes approximately 90% of all MIs in Sweden [17]. For this study we utilized two of SWEDEHEART's sub-registers: RIKS-HIA (Register of Information and Knowledge about Swedish Heart Intensive Care Admissions) and SEPHIA (Secondary Prevention after Heart Intensive Care Admission). The RIKS-HIA register includes patients who have had an MI in Sweden and records information regarding the episode, such as relevant data on medical history, admission, symptom onset, in-hospital treatments provided, and discharge information, including medications prescribed. The SEPHIA register began in 2005, and as of 2014, coverage was approximately 80% [18]. Only individuals aged 74 years and younger are eligible to participate. Those who enroll are interviewed on two occasions: approximately 6–10 weeks (Interview 1) and 12–14 months (Interview 2) after the MI event.

SWEDEHEART data were linked to the Swedish Prescribed Drugs Register, which includes information on dispensed medications, and National Patient Register, which records all inpatient and outpatient hospital visits, with the exception of primary care visits. This study was conducted with approval from the regional ethics committee in Uppsala, Sweden (Dnr: 2013/478).

2.2. Sample and observation periods

We selected individuals with a first MI who had received a first-time statin prescription at discharge. To exclude participants who had previously received a statin prescription, we removed those with registered statin use upon admission, as well as those who had a record of a statin pickup prior to the MI event. This was done to ensure that we could evaluate a homogeneously statin-naïve population not been previously exposed to potential side effects or with issues of non-adherence. We also excluded individuals who did not participate in SEPHIA.

We used three observation periods (OP) for adherence: 1) from Interview 1 (approximately 6–10 weeks after the MI) to Interview 2 (approximately 12–14 months after the MI), 2) the year following Interview 2, and 3) two years after Interview 1, or the complete OP for adherence (Fig. 1). Number of days in the each period was calculated based on time between recorded interview dates or the end date stipulated by the study design. The first included patients who had their first follow up after the MI before January 1, 2013. This resulted in a sample of 15,154 participants after excluding individuals who died or had missing data on exposure, outcome, or any of the confounders. The second and complete OPs included individuals who had the first interview after the MI before January 1, 2012 to ensure all participants had the respective follow-up time's worth of recorded refills, which resulted in a sample of 10,674 and 12,357, respectively, after excluding those who died or had missing values on any of the study covariates. Appendix 1 shows a flowchart of the number of individuals excluded and those with missing values.

2.3. Outcome

To calculate statin adherence, we used the medication possession ratio (MPR) measure:

$$MPR = \frac{Number\ of\ pills\ obtained}{Number\ of\ days\ in\ OP}$$

For this study data on dosage was missing; therefore, we assumed that each individual was prescribed one statin pill per day as has been reported true for approximately 98% of prescriptions [19]. For OP 1, we measured adherence for the time between each patient's follow-up interviews, approximately one year after the MI event. We calculated the time between those two dates and calculated the number of pills distributed during this period. The reimbursement system in Sweden allows individuals to refill prescriptions for up to a three-month's supply at a time. Because of this we had to account for any leftover pills dispensed immediately after the MI and before Interview 1. We used the amount of surplus medication they had obtained and added it to the number of pills for our time period of interest. If individuals did not have enough pills to cover the initial MI-Interview 1 period, we did not add or subtract from their adherence calculation. Fig. 2 shows sample calculations for two hypothetical patients. This same process was repeated for the second and complete OPs. To be considered adherent, individuals had to have taken out pills covering > 80% of the days, which is the usual convention for cardiovascular medication adherence studies [11]. Lastly, some patients got a supply of their daily medications automatically sent to them from their pharmacy every 14 days. We excluded these individuals as they could artificially increase adherence [19].

During Interview 2, participants reported whether or not they regularly took a variety of medications prescribed at discharge, including statins. Although interviewers may have this information written on each participant's chart, interviewers were to ask and write down the patient's answer. We used this variable to compare adherence calculated from the pharmacy register with self-reported adherence.

2.4. Exposure

To characterize emotional distress, we used the European Quality of Life Five Dimensions questionnaire (EQ-5D). This instrument consists of five questions, each with a three-item ordinal response scale. The five questions are designed to measure mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [20]. We utilized the anxiety/depression dimension, which consists of the following three alternatives: “1: I am not anxious or depressed,” “2: I am anxious or depressed to some extent,” and “3: I am extremely anxious or depressed” [20]. Overall, the EQ-5D has shown to have good reliability and validity in over 60 studies of cardiovascular disease [21]. The anxiety/depression dimension has shown moderate associations with established measures of depression and anxiety, such as the Mini International Neuropsychiatric Interview, the Beck Anxiety Inventory, and the Beck Depression Inventory [22–27]. Additionally, one study found that individuals with both anxiety and depression were more likely to report some anxiety or depression on the EQ-5D than those with anxiety or major depressive disorder alone. However, those with only anxiety or depression were