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Treatment Adherence to Drug Therapy in Patients with Stable Coronary Artery Disease During the COVID-19 Pandemic

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The new coronavirus infection (COVID-19) pandemic and the subsequent quarantine measures, particularly home isolation of the population, could have seriously affected the quality of pharmacotherapy and adherence to it by patients with chronic non-communicable diseases.

Aim. To assess the dynamics of adherence to pharmacotherapy by patients with stable coronary artery disease (SCAD) in self-isolation during the COVID-19 pandemic.

Material and methods. To accomplish the aim of the study, we selected 39 patients with SCAD who previously completed the ALIGN study, the purpose of which was to align patients' medical therapies according to current clinical guidelines. From May 05, 2020, to May 14, 2020, a telephone survey was conducted of 39 patients with SCAD (37, 94.8%) males, mean age 67.6±8.5 years). After one year of participation in the ALIGN study, 87.1% of the patients were adherent to their prescribed pharmacotherapy. Adherence (overall and to specific medications) was assessed by means of the original adherence scale, which made it possible to identify violations in taking medications (non-adherence to the intake regime or discontinued intake of medications), and the main reasons for adherence violation were established. Adherence registered during the telephone survey at the time of the COVID-19 pandemic was compared to that obtained during the last time the patient participated in the ALIGN study.

Results. During the period of home isolation, a substantial decline in the adherence of patients to pharmacotherapy was revealed. The percentage of adherent patients decreased from 87% to 54% due to an increase in the number of patients who stopped taking several or all of the recommended drugs during home isolation (p=0.024). The overall rate of adherence during the COVID-19 pandemic appeared to be even worse than before the start of the ALIGN study. A comparative analysis of subgroups with and without a decline in adherence revealed a trend suggesting that higher patient education (p=0.067) or previous percutaneous coronary intervention (p=0.063) can be considered a protective factor associated with fewer violations in adherence during the COVID-19 pandemic. Analysis of adherence to specific drugs showed that during self-isolation there was a decrease in adherence to antiplatelet drugs (p=0.047) and to statins (p=0.055). Adherence to beta-blockers, renin-angiotensin-aldosterone system inhibitors and dihydropyridine calcium antagonists remained unchanged.

Conclusion. In patients with SCAD during the period of home isolation in the COVID-19 pandemic and associated difficulties in contacting the attending physician, there was a decline in adherence and an increase in the number of patients who stopped taking several or all prescribed drugs.

Keywords: adherence, pharmacotherapy, stable coronary artery disease, COVID-19 pandemic, home isolation, telephone survey.

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Introduction

The new coronavirus infection COronaVIrus Disease 2019 (COVID-19) pandemic and the subsequent quarantine measures, particularly the home isolation of the population, have seriously influenced the lifestyle of people, especially those suffering from chronic non-communicable diseases, along with other problems that may have affected the quality of their ongoing pharmacotherapy. For various reasons, during the COVID-19 pandemic, these patients may have had a number of problems accessing an appropriate specialist or receiving or purchasing medications that they regularly take.

A number of recently published studies have reported the occurrence of adherence problems in dermatology patients and in patients with autoimmune inflammatory rheumatic diseases [1,2]. The purpose of the present study was to assess changes in adherence to continuous therapy in patients with chronic stable coronary artery disease (SCAD) in home isolation during the COVID-19 pandemic.

Material and methods

To accomplish the aim of the study, we selected 39 patients with SCAD who had previously completed their participation in the TherApy study in stabLe Coronary Artery dIsease Patients According to Clinical GuideliNes (ALIGN) study (NCT04162561 at ClinicalTrials.gov), which is a prospective cohort study of treatment adherence in patients with SCAD after correction of their recommended pharmacotherapy in accordance with clinical guidelines for the treatment of patients with SCAD. The main purpose of the ALIGN study is to assess the effectiveness of the pharmacotherapy depending on treatment adherence. The study involved primary patients with proven SCAD who were recruited from the outpatient PROFILE registry of patients with cardiovascular diseases and associated risk factors [3]. All patients gave informed consent to include personal data in the registry and to participate in the ALIGN study and surveys related to it.

The ALIGN study protocol and questionnaires were approved by an independent ethics committee. In addition, an independent ethics committee reviewed and approved an additional telephone survey of adherence during the COVID-19 pandemic in patients who had already completed the study.

In the period from May 5 to May 14, 2020, a telephone survey was performed to assess adherence to cardiovascular drug therapy during the outbreak of the new coronavirus infection and home isolation in patients who had completed their participation in the ALIGN study (n=39).

Adherence was assessed using the National Society for Evidence-based Pharmacotherapy adherence scale [4]. Patients were considered to be adherent if they fully complied with doctors' recommendations in relation to pharmacotherapy. Any violation of the intake regime or self-changing of the drug daily dose was considered partial adherence. Patients who completely stopped taking one or more drugs were considered to be non-adherent. If a dichotomous division into subgroups was necessary, patients with partial adherence and non-adherent patients were grouped into one subgroup of non-adherent patients. In addition, phone survey participants were divided into two subgroups: 1) those with a decline in adherence and 2) those with no change in adherence during the period of self-isolation against the background of the COVID-19 pandemic. Adherence was determined both to the entire pharmacotherapy (overall adherence) and separately to the drugs of each group (antiplatelet drugs, statins, beta-blockers, etc.).

Of the 71 patients included in the ALIGN study, only 39 completed all three planned visits (the inclusion visit and the 3- and 12-month follow-up visits) before the beginning of the home isolation period. Accordingly, only these patients were interviewed by telephone during the COVID-19 pandemic. During telephone contact, patient adherence to the recommended cardiovascular pharmacotherapy (overall and to specific drugs) and changes in the conditions of self-isolation were determined. Thus, the study cohort included 37 men (94.8%) and 2 women; the average age of the patients was 67.6±8.5 years.

The study scheme is shown in Figure 1.

Statistical analysis was performed using SPSS Statistics 23.0 software (IBM, USA). For descriptive statistics of quantitative variables with normal distribution, the means and standard deviation (M±SD) are presented. Qualitative variables are represented as percentages. For comparisons of the quantitative data, the Mann-Whitney U test and Kruskal-Wallis test were used. For analytical statistics of the qualitative variables, we used the Pearson's chi-squared test and the Fisher exact criterion (for 2×2 tables), and McNemar's test for related samples, calculating the odds ratio (OR) with a 95% confidence interval (CI), and the z-criterion for comparing proportions.

Results

The characteristics of patients who took part in the telephone survey to assess adherence during the COVID-19 pandemic are shown in Table 1.

By the end of the one-year follow-up of the ALIGN study, 87.1% of patients were adherent to the recommended cardiovascular pharmacotherapy. The dynamics of overall adherence based on the results of the National Society for Evidence-based Pharmacotherapy adherence scale assessed during the COVID-19 pandemic are shown in Figure 2. During the period of home isolation, a substantial decline in patient adherence to pharmacotherapy was registered. The percentage of fully adherent patients decreased by one-third (from 87.1% to 53.8%) due to an increase in the number of non-adherent patients who stopped taking several or all of the recommended medications (p=0.024). Two patients (5.1%) completely stopped the recommended pharmacotherapy. Notably, treatment adherence during the COVID-19 pandemic appeared to be even worse than at the baseline visit upon patient inclusion in the ALIGN study (Figure 2).

When using a dichotomous gradation for the results of the National Society for Evidence-based Pharmacotherapy adherence scale, it was demonstrated that during the period of self-isolation, the rate of patient non-adherence to the recommended drug treatment increased almost six-fold: OR= 5.8 95% CI (1.9; 18.0), p=0.002.

A comparison of the subgroups of patients with decreased adherence and unchanged adherence revealed a trend showing that a higher education status (p=0.067) or a history of percutaneous coronary intervention (p=0.063) was a protective factor asso-

ciated with the absence of decreased adherence during self-isolation. The differences between subgroups did not reach statistical significance, which may be due to the small number of survey participants and/or insufficient statistical capacity of the study. Other clinical and demographic factors, in particular, gender, age, and the presence of concomitant diseases, did not significantly affect the dynamics of adherence. The results of the assessment of adherence to specific drug groups are presented in Table 2.

There was a decrease in adherence to antiplatelet drugs (p=0.015) and statins (p=0.045). The intake of beta-blockers, renin-angiotensin-aldosterone system inhibitors and dihydropyridine calcium channel blockers remained unchanged.
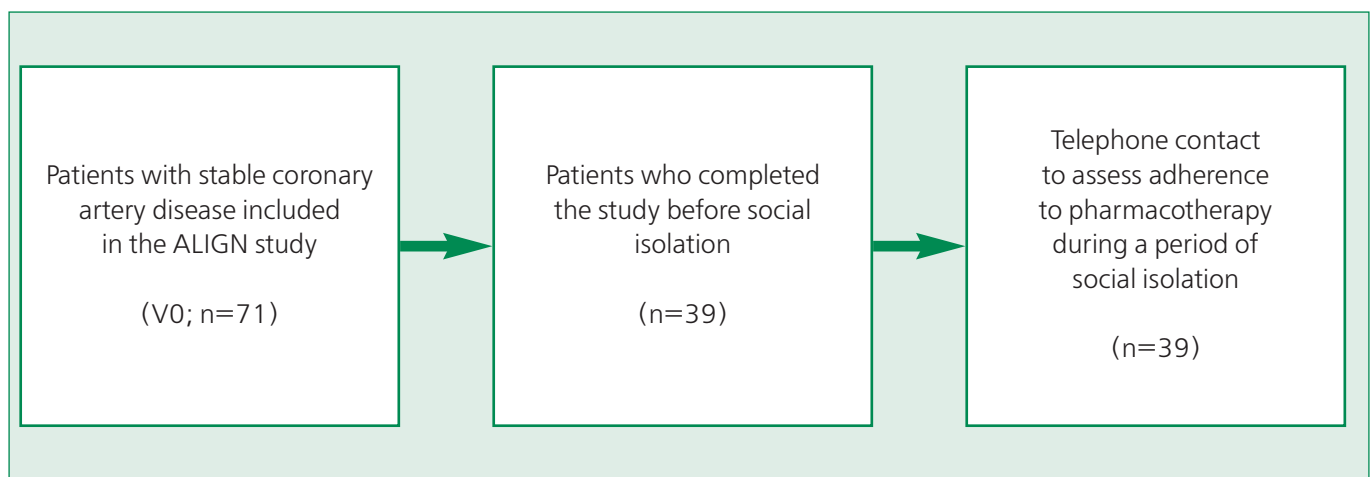
Table 1. Clinical and demographic characteristics of patients (n=39)

Patient characteristics	Value
Men, n (%)	37 (94.8)
Age, years	67.6±8.5
AMI in history, n (%)	22 (56.4)
Stable angina, n (%)	26 (60.0)
Hypertension, n (%)	37 (94.8)
Diabetes mellitus, n (%)	9 (23.1)
CHF, n (%)	16 (41.0)
AF, n (%)	8 (20.5)
PCI in history, n (%)	22 (56.4)
CABG in history, n (%)	11 (28.2)

Data are presented as M±SD, unless indicated otherwise

AMI – acute myocardial infarction, CHF – chronic heart failure,

AF – atrial fibrillation, PCI – percutaneous coronary intervention,

CABG – coronary artery bypass surgery

Figure 1. Scheme of the study

Patients with stable coronary artery disease included in the ALIGN study

(V0; n=71)

Patients who completed the study before social isolation

(n=39)

Telephone contact to assess adherence to pharmacotherapy during a period of social isolation

(n=39)

Discussion

Crisis situations, including the COVID-19 pandemic, reveal new facets in the problem of adherence to treatment by patients with various chronic non-communicable diseases, including cardiovascular diseases. During the pandemic, there was a decrease in the ability of patients to visit doctors, an increase in stressful situations and an increase in various psychological/mental disorders, each of which can diminish patients' adherence to prescribed pharmacotherapy. Issues of drug supply to the population and the need to expand the use of telemedicine technologies were of particular relevance during the COVID-19 pandemic [5]. To date, a limited number of studies have been performed to examine adherence issues in patients with chronic non-communicable diseases during the period of home isolation during the COVID-19 pandemic.

In the study of G.E. Fragoulis et al. [2], decreased adherence was found in patients with autoimmune inflammatory rheumatoid diseases during the pandemic. The main barriers to adherence in these patients were the fear of immunosuppression in a difficult epidemiological period, insufficient provision of medicines (especially for the non-adherence of patients due to hydroxychloroquine deficiency), acute respiratory infections and side effects of drugs. Notably, however, adverse effects were among the most frequent causes of pharmacotherapy termination not associated with the pandemic and the significance of these concerns did not diminish during the period of home isolation. However, it is evident that there are additional barriers to adherence during a pandemic. According to our data, during the period of home isolation, the level of patient adherence to cardiovascular drug therapy was even lower than it had been during their participation in the ALIGN study. The possible explanation for the lower adherence during the COVID-19 pandemic, among other barriers to adherence, was the lack of regular contact with a doctor during home isolation and are sulting decrease in motivation to regularly follow medical recommendations for pharmacotherapy.

Similar to the findings by Greek researchers [1], who conducted a telephone survey to assess the adherence of 237 patients with psoriasis, we did not find significant associations between any clinical or demographic indicators and adherence disorders in patients with SCAD during the period of self-isolation. However, there was a trend suggesting that patients higher education status (p=0.067) or percutaneous coronary intervention (p=0.063) can be considered a protective factor associated with the fewer adherence violations.

In contrast to the results of telephone surveys [1,2], including our own, a cross-sectional study of German authors revealed increased adherence to cardiovascular and antidiabetic pharmacotherapy during
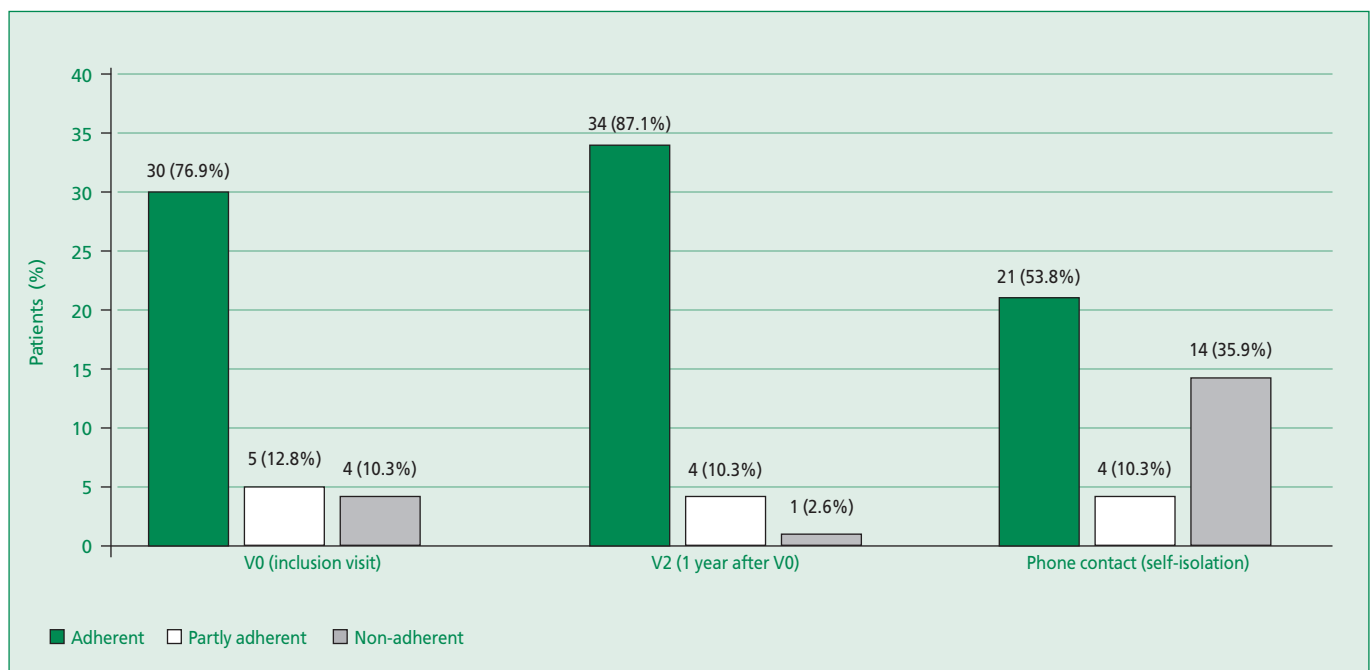

Figure 2. Changes of adherence to pharmacotherapy before and during the period of social isolation in the COVID-19 pandemic

Table 2. Adherence to specific drug classes

Drugs	Adherence at V2 of the ALIGN study, n (%)	Adherence during the period of self-isolation, n (%)	p
Antiplatelet drugs, n (%)	37 (94.8)	30 (77.0)	0.015
Statins, n (%)	39 (100)	34 (87.2)	0.045
Beta-blockers, n (%)	34 (87.2)	32 (82.0)	0.29
ACE inhibitors, n (%)	26 (66.7)	26 (66.7)	1.0
ARB, n (%)	9 (23.0)	9 (23.0)	1.0
Dihydropyridine CCB, n (%)	12 (30.8)	12 (30.8)	1.0
NOAC, n (%)	8 (20.5)	7 (18.0)	0.62

ACE – angiotensin-converting enzyme, ARB – angiotensin II receptors blockers, CCB – calcium channel blockers, NOAC – non-vitamin K antagonist oral anticoagulants

the COVID-19 pandemic. However, this conclusion was based on an analysis of data on the implementation of prescriptions for cardiological and antidiabetic drugs by patients in the first quarter of 2020 compared to the same period in 2019 [6]. The results showed that the number of prescriptions for cardiovascular and antidiabetic drugs issued at the beginning of 2020 increased by 18-30%. It seems that the use of indirect methods of diagnosing adherence in this study (telephone interview and analysis of the number of prescriptions written) were the reasons for the discrepancy in results.

A significant problem that arose at the beginning of the COVID-19 pandemic was the possibility of continuing treatment with ACE inhibitors due to the detected tropism of the SARS-CoV-2, the virus that causes new coronavirus infection, to the ACE receptor. However, this problem was resolved quickly. No clinically relevant data demonstrated a negative effect of ACE inhibitors on the infection or course of COVID-19, and no increased risk of cardiovascular complications was shown. This is why leading cardiological societies issued recommendations highlighting the irrationality of discontinuing ACE inhibitors or angiotensin II receptor blockers for the prevention and treatment of COVID-19 in patients with cardiovascular diseases [7,8]. The results of our study showed that data on the dangers of prescribing these drugs did not affect patient adherence since no cases of withdrawal or discontinuation have been reported.

Conclusion

In patients with SCAD during the period of self-isolation during the COVID-19 pandemic and the associated lack of constant contact with the attending physician, there was a decline in adherence and an increase in the number of patients who stopped taking several or all prescribed drugs. The most pronounced negative dynamics were observed in adherence to antiplatelet agents and statins.

Limitations of the study: The small number of patients who took part in the telephone survey and, consequently, the small statistical power of the study, probably did not allow us to determine all the significant factors of non-adherence. However, a number of trends were identified in the association of certain factors with impaired adherence to pharmacotherapy. These findings allow us to formulate a number of null hypotheses that need to be verified in further research.

Relationships and Activities: none.

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