Original Article

Motivational interviewing to support LDL-C therapeutic goals and lipid-lowering therapy compliance in patients with acute coronary syndromes (IDEAL-LDL) study: rationale and design

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Abstract

Background: Achieving low-density lipoprotein cholesterol (LDL-C) target levels after an acute coronary syndrome (ACS) is of paramount importance, and is often burdened by undertreatment and medication or lifestyle non-adherence issues.

Objective: We examined the effect of a patient-centered, physician-led motivational intervention following ACS on relevant secondary prevention aspects.

Methods-design: The IDEAL-LDL is a single-center, randomized controlled clinical trial, conducted among patients hospitalized due to an ACS. Following discharge, all patients undergo a baseline assessment of lipid profile. Patients in the intervention group receive an in-person educational session and an informative leaflet, and also undergo two phone-based, motivational interviewing sessions at 1 and 6 months. These interventions emphasize on LDL-C goals, adherence to lipid-lowering medication, and healthy dietary-lifestyle habits, and are not provided to patients in the control group, who receive usual care. At 12 months after each patient's discharge, an in-person interview and lipid profile reassessment are performed. The primary outcomes are the assessment of LDL-C goal achievement (<70 mg/dL or >50% reduction from baseline levels) from baseline to 1 year and changes in medication adherence. Secondary outcomes relate to the incidence of the composite outcome of cardiovascular death, nonfatal myocardial infarction/stroke, need for myocardial revascularization, and recurrent hospitalization during the follow-up period.

Discussion: This paper describes the protocol, design, and rationale for key methodology for an ongoing clinical trial featuring a simple and feasible intervention. Similar adherence efficacy trials have not led to sufficient improvements, and there remains a gap regarding how adherence interventions should be implemented into clinical care.

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of LDL-C, underlining the need for more intensive cholesterol management.[13]

Interventions aiming at improving adherence to treatment have shown benefit in secondary prevention of various disease entities. Previous risk factor modification programs based on telemedicine seem effective in altering lifestyle variables, as well as in motivating patients to participate substantially in promoting health.[14,15] In the case of prior ACS, a paucity of relevant trials has been mostly proven ineffective in improving the patients’ lipid profile, leading researchers to claim that a ceiling effect may have been reached.[16] Nonetheless, contiguous interventions have resulted in reduced hospital readmissions.[17,18]

We set out to integrate a randomized controlled trial study into clinical care of ACS patients. Our primary hypothesis is that the target LDL-C goals can more effectively be achieved through a structured patient education intervention. We considered this intervention in the form of motivational interviewing and regular post-discharge follow-up by appropriately trained health care personnel. In the intervention group, we expect a greater reduction from baseline lipid levels compared with the standard of care, over a 12-month period, along with better adherence to statin therapy. Secondarily, we aim to test the effects on outcomes, such as cardiovascular mortality and morbidity and readmission rates along with the magnitude of cardiovascular clinical adverse events developing within 12 months after ACS.

2. Methods

2.1. Study design and setting

The IDEAL-LDL study is a two-arm, prospective, single-center, outcome-blinded, randomized controlled study. The study is conducted in AHEPA University Hospital, whose care network covers a population of over a million inhabitants within the second largest city in Greece. The trial is registered in ClinicalTrials.gov (Identifier: NCT02927808) and received approval from the Aristotle University Ethics Committee, according to the current version of the Declaration of Helsinki (2013).

2.2. Study population

This study is enrolling adult patients from a tertiary-care cardiology department inpatient setting in Thessaloniki, Greece.

2.2.1. Inclusion criteria

(i) Documented diagnosis of ACS on admission, consistent with the Third Universal Definition of Myocardial Infarction (2012).[19] ACS was diagnosed when clinical evidence of acute myocardial ischemia was present, along with detection of a rise and/or fall in high sensitivity cardiac troponin-T (hs-cTnT), with at least one value above the 99th percentile upper reference limit (URL) and at least one of the following:

a. Symptoms of ischemia;

b. New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB);

c. Development of pathological Q waves in the ECG;

d. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality;

e. Identification of a coronary thrombus by angiography.

Because we only use cardiac troponin-T (cTnT) as a biomarker of myocardial injury, our method to code ACS is also consistent with the recently published Fourth Universal Definition of Myocardial Infarction (2018), which focuses solely on cTnT over the rest biomarkers.[20]

(ii) Previously or newly prescribed lipid-lowering medication, as recommended in the European Guidelines of Dyslipidemias (2016),[4,5] unless contraindicated

(iii) Age more than 18 years, no upper age limit

(iv) Capable of providing informed signed consent or via a legally authorized representative and participating in all associated study activities.

2.2.2. Exclusion criteria

(i) Unable to communicate through telephone for study interviewing

(ii) Contraindication to statin therapy or any medical disorder that would interfere with completion or evaluation of clinical study results.

2.3. Study overview

All the patients who present to the hospital with a diagnosis of ACS are screened by either the principal investigators or delegated study personnel who assess eligibility for enrollment. Eligible subjects are approached and contacted in-person at hospital discharge by a principal investigator or his/her authorized designee in order to obtain informed signed consent.

2.4. Baseline assessments

Data collection concerning baseline assessment is performed at the bedside, on the day of discharge. Delegated study personnel assess enrolled subjects regarding multiple profile parameters, including contact information, demographics, level of education, alcohol consumption, smoking and physical activity status, and full medical and family history with emphasis on the cardiovascular history. Additionally, the personnel assess somatometric parameters (height, weight, and body mass index) using standardized procedures. Detailed information about the ACS that led to the subject’s hospitalization (e.g., onset, type and duration of symptoms, time of arrival at the hospital, type of treatment, results of potential intervention, etc.) and medication during and after hospitalization are also inquired, while baseline lipid profile is evaluated. All relevant data are coded in predefined templates, later to be transcribed for statistical analysis.
2.5. Randomization

Following discharge, patients are assigned to one of two treatment groups. A simple randomization procedure (computerized random numbers) to 1 of 2 treatment groups in a 1:1 ratio is performed by an independent authorized researcher, who is uninvolved with the patients’ care.

Patient assignments are placed in sealed opaque envelopes. As it is common for most behavioral interventions, neither the patients nor the study personnel will be blinded to the intervention. However, the allocation procedure will be concealed from researchers analyzing data and outcomes.

2.6. Treatment groups

The study flow is depicted in Fig. 1.

- Control Group (A)

Subjects in group A receive usual care, the same as all the patients presenting to the hospital with an acute coronary syndrome. The clinical care team (physician, physician’s assistants, and/or nursing staff) provides basic counseling and reviews about the discharge medication. New medication will be prescribed, if needed, in accordance with the discharge letters. Patients assigned to the control group will be contacted for a pre-specified in-person interview at 12 months after discharge.

- Intervention Group (B)

Subjects in group B receive usual care and an additional, in-person contact, by a trained study physician or delegated study personnel at hospital discharge. During this contact, the subject is given a leaflet entitled “Information Leaflet about LDL Cholesterol” that aims to educate them about the risks of high LDL-C and the importance of adherence to lipid-lowering medication. The leaflet is created in Greek language, pertinent to the native population studied. It consists of figures and bullet points; thus, it is easy to read for all patient ages. Those included are the basic information regarding the types of cholesterol, dietary instructions, and healthy lifestyle motivation, in the form of simple recommendations. The patient is asked to read the leaflet carefully and the study physician answers any relevant questions.

Patients assigned to the intervention group (B) are contacted through telephone for a pre-specified interview at 1 month, 6 months after discharge, and for an in-person interview at 12 months after discharge. A study physician or trained delegated study personnel conduct the interview. During these telephone sessions, a standardized case report form with somatometric factors, clinical events (e.g., recurrent acute coronary syndrome, bleeding, stroke, death, etc.), and medication are recorded. Adherence to statin medication is evaluated during 12 months interview session. The simple question “In the past month, how often do you take your medications as prescribed by your doctor?” is being utilized in order to assess adherence and nonadherence as a binary outcome. Possible answers are “All of the time” (100%), “Nearly all of the time” (90%), “Most of the time” (75%), “About half of the time” (50%) or “Less than half of the time” (<50%), non-adherence was designated as 75% of the time or less. There is proof that this self-reported measure of adherence is adequately capable of pinpointing patients at risk for major adverse cardiovascular events.21 The research assistant conducting the interview also cares to emphasize the importance of the achievement of LDL-C therapeutic goal (LDL-C <70 mg/dL). Patients who are not capable of attending the 12-month in-person interview are contacted through telephone to assess the secondary outcomes. Counseling concerning other modifiable cardiovascular risk factors such as smoking cessation and weight loss will be performed in every patient-physician interview. No other medical consultation and intervention is provided during the telephone interviews. However, patient questions related to lipid-lowering therapy are recorded and reviewed by a physician within a reasonable time. If any of these questions is deemed relevant to patient’s safety, the study physician communicates with the patient in-person (Fig. 2).

All the subjects are informed that participating in the study is not supposed to replace standard medical care. Patients in both groups are encouraged to contact the study physician for any question directly related to the study.

2.7. Follow-up assessments

The pre-specified in-person interview at 12 months after discharge includes, both for Control Group (A) and Intervention Group (B), the completion of a standardized case report form (same

Fig. 1. Overall IDEAL-LDL study flow.

Fig. 2. IDEAL-LDL intervention program study flow.
as the one used during the 1 month and 6 months telephone sessions) and a small series of blood measurements including LDL-C, high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), and triglyceride (TG) levels.

2.8. Study endpoints

The primary objectives are to test whether the added intervention of motivational interviewing coupled with an educational leaflet provided by a trained physician or delegated authorized study personnel, contributes to the achievement of LDL-C therapeutic goals (LDL-C <70 mg/dL or >50% reduction from baseline) 12 months after hospitalization of patients diagnosed with an ACS and to evaluate post-ACS patients’ adherence to medication.

Our secondary objectives, assessed as composite outcomes, include ascertaining whether the intervention reduces total coronary heart disease mortality, recurrent nonfatal myocardial infarction (MI), stroke, need for myocardial revascularization, and recurrent hospitalization in patients with ACS.23-25 Supplementary analyses will be performed in the group of patients with LDL-C >190 mg/dL, i.e., possible familial hypercholesterolemia (FH), to examine lipid-lowering goal attainment and medication adherence.3 The intervention’s effect in attenuation of other reversible risk factors, such as smoking cessation and weight loss will also be assessed (Table 1).23-27

2.9. Statistical issues

2.9.1. Analysis

The primary analysis will consist of comparing the results of the change in LDL-C from baseline to 12 months between the groups of patients in the usual care group compared with the intervention group. The statistical analysis will be performed using a two-sample t-test, and two-sided 95% confidence intervals will be used to describe the treatment differences. To test for the intervention effect while controlling for different patient characteristics, an analysis of covariance will be used.

2.9.2. Sample size calculation

The total number of subjects that will be enrolled in the IDEAL-LDL study is estimated approximately as 300, as a sample size of 296 is required to have 90% power to detect an increase in the primary outcome measure from 20% in the control group to 40% in the experimental group, given an anticipated dropout rate of 10%.

3. Discussion

Considering the extremely high prevalence of dyslipidemia and CAD presently, it is easy to understand why lipid-lowering therapies are currently in the center of attention.20,21 The dogma “the lower the LDL-C, the better” in secondary prevention has become very popular among clinicians, as it has been proven that the role of LDL-C in pathogenesis and epidemiology of cardiovascular disease (CVD) is fundamental.22 Nonetheless, failure in reaching the desirable LDL-C targets is common among patients with ACS and improved adherence could play a key role in reversing this trend.23-25 Previous studies involving telephone-based interviews, designed to determine whether this type of intervention actually enhances adherence to LDL-C targets have shown encouraging results, but it is yet to be fully proven.23-25 The compelling benefit of our study is the duration and the intensity of the intervention, as analogous studies either extend on a shorter period of time or consist of more infrequent telephone sessions. Additionally, the fact that physicians constitute the personnel interacting with patients is expected to strengthen the study’s capacity. Patients rely prodigiously on doctors’ opinion, and are expected to obtain in-depth answers and proper therapy adjustments on the basis of the patient-caregiver interaction.23-25

There are no anticipated adverse events and risks directly related to the study. The IDEAL-LDL study is not initially intended to change or replace standard patient medical care, thus new insights in post-ACS patient follow up may be indicated. Notwithstanding, there are potential adverse events and risks related to statin therapy.

Limitations of the study include its single-center nature, which hinders reproducibility in different settings. Moreover, the study population is restricted to Greek-speaking subjects due to the challenges of conducting the scripted and oral intervention in other languages besides Greek. The anticipated dropout rate may compromise our study’s validity. We intend to minimize this rate by keeping multiple telephone numbers for each subject. Nevertheless, alterations in contact information or deaths occurring during follow-up pose unavoidable problems. Additionally, some variability in the applied intervention may ensue due to the different practice styles of involved study personnel interacting with patients. Of note, the study is not powered for detecting secondary outcomes, which increases the risk that a significant difference may not be shown, even if such a difference exists (type 2 error).

Collectively, the proposed research aims to test the effectiveness of motivational interviewing for improving secondary prevention of cardiovascular disease due to ACS. It relies upon a patient centered approach, easily applied in most clinical environments. Demonstrating successful integration into routine practice would be an initial goal. Whether this particular intervention contributes to the reduction of LDL-C and major, ACS-related cardiovascular events, remains to be seen. Ultimately, should the trial’s endpoints prove statistically significant, IDEAL-LDL has the potential to change the standard of care, at least in its native setting.

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