

Hypertriglyceridemia, an Underestimated Cardiovascular Risk Factor: An Epidemiological Study of the Rome Area

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Abstract

Introduction Hypertriglyceridemia (triglycerides ≥ 200 mg/dL) is a major cardiovascular risk factor. Despite the high incidence of this condition in the Italian population, epidemiological information remains limited.

Aim To analyze a large database of clinical charts from general practitioners in the Rome area of Italy.

Methods In this study, the DATAMEG database of patients treated in the Rome area between 2000 and 2015 was analyzed. The database was searched for information on (1) all patients diagnosed with hypertriglyceridemia, (2) all prescriptions for the treatment of hypertriglyceridemia, and (3) all patients who had an acute myocardial infarction.

Results The overall prevalence of hypertriglyceridemia was 4.4% (3647/82,595). Among patients followed from January 1, 2015 onwards, 2786/55,345 (5.0%) were diagnosed with hypertriglyceridemia. Of these, 418 (15.0%) received at least one prescription of triglyceride-lowering treatment. Over the same period, 1653 patients had at least three measurements of triglycerides ≥ 200 mg/dL, with only 357 (21.6%) receiving at least one prescription of triglyceride-lowering drugs in the year following the last measurement. Furthermore, 513 patients had at least one measurement of ≥ 500 mg/dL. Of these, only 246 (48.0%) received at least one prescription of

triglyceride-lowering drugs in the year following the last measurement. In total, 3485 patients had an acute myocardial infarction (prevalence, 4.3%) in 2015. Of these, only 288 (8.3%) received at least one prescription of triglyceride-lowering drugs in the year following this event.

Conclusion These findings confirmed a pattern of inadequate treatment of hypertriglyceridemia in the Rome area.

Keywords Epidemiological study · Hypertriglyceridemia · Lipid lowering treatment · Myocardial infarction

1 Introduction

Cardiovascular diseases represent the main cause of death in the Italian population and are associated with a major healthcare burden [1]. Many risk factors for cardiovascular disease, such as obesity, hypertension, and dyslipidemia, are modifiable [2]. Therefore, early detection of these risk factors is of crucial importance both for general practitioners (GPs) and cardiologists.

The introduction of statins has led to a marked decrease in the incidence of cardiovascular events in patients with hyperlipidemia [3]. Accordingly, reduction of low-density lipoprotein (LDL) cholesterol levels is considered fundamental in the prophylaxis of cardiovascular diseases [4]. Despite this, data from a number of clinical studies indicate that a residual risk of cardiovascular events remains, even after LDL cholesterol levels have been corrected [5, 6]. This is likely caused by triglyceride-rich lipoprotein remnants (TRLRs) that, due to their small size, can penetrate the arterial wall. Accumulation of TRLRs leads to the formation of an atherosclerotic plaque [2].

Hypertriglyceridemia (defined as a plasma concentration of triglycerides of ≥ 200 mg/dL) is a condition frequently

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encountered in clinical practice. Data from the Italian Institute of Health suggest that approximately one in three Italian adults have elevated levels of triglycerides [1]. Hypertriglyceridemia can be either primary or secondary to a number of diseases, including obesity, type 2 diabetes, and the metabolic syndrome. In a large meta-analysis of prospective clinical trials, hypertriglyceridemia was identified as a strong and independent predictor of cardiovascular risk [7]. Therefore, control of hypertriglyceridemia is an important therapeutic objective in the prevention of cardiovascular events [8].

Epidemiological information on hypertriglyceridemia and its treatment in Italy remains limited, despite the high incidence of this condition and its relevance as a risk factor for cardiovascular disease. The aim of this study was to address this gap in the literature by analyzing a large database of clinical records from GPs in the Rome area.

2 Methods

The DATAMEG database contains anonymized clinical charts of >80,000 patients treated at the general medicine wards in the Rome area, about 55,000 of whom are still being followed. Records dating from January 1, 2000 to December 31, 2015 were analyzed (EC authorization protocol 456/12).

The database was searched for information on: (1) all patients diagnosed with hypertriglyceridemia (blood concentration of triglycerides of ≥ 200 mg/dL) [International Classification of Diseases, ninth revision (ICD-9), codes 272.1, 272.2, 272.3 or 272.4]; (2) all prescriptions for the treatment of hypertriglyceridemia [World Health Organization Anatomical Therapeutic Chemical (ATC) classification system codes ATC C10AB*, C10AD*, or C10AX06]; (3) all patients who had an acute myocardial infarction (MI) (ICD-9 410, 411, 413 or 414).

Search results were analyzed using descriptive epidemiology methods with the following aims: (1) to determine the prevalence of hypertriglyceridemia, independently (primary) or secondary to a diet rich in fats and carbohydrates, abuse of alcohol, diabetes, metabolic syndrome, obesity, drugs such as beta-blockers, thiazide diuretics, estrogens, progesterone, steroids, tamoxifen, and antiretrovirals; (2) to determine the number of patients diagnosed with hypertriglyceridemia, who received in 2015 at least one prescription of drugs for the treatment of hypertriglyceridemia; (3) to determine the number of patients with at least three measurements of triglyceride concentrations of ≥ 200 mg/dL who received at least one prescription of indicated drugs in the year following the last measurement; (4) to determine the number of patients with at least one measurement of triglyceride concentrations of ≥ 500 mg/dL who received at

least one prescription of indicated drugs in the year following the last measurement; (5) to determine how many patients diagnosed with acute MI received at least one prescription of triglyceride-lowering drugs in the year following this event. Epi Info 7 software was used for this analysis.

3 Results

In total, 3647 patients in the database received a diagnosis of hypertriglyceridemia. The overall prevalence of hypertriglyceridemia was 4.4% (3647/82,595), and 53 and 47% of those affected were male and female, respectively.

Among the patients followed from January 1, 2015 onwards, 2786/55,345 (5.0%) were diagnosed with hypertriglyceridemia. Of these, 418 (15.0%) received at least one prescription of a triglyceride-lowering treatment during the year 2015.

Over the same period, 1653 patients had levels of triglycerides ≥ 200 mg/dL on at least three measurements. Of these, only 357 (21.6%) received at least one prescription of triglyceride-lowering drugs in the year following the last measurement (Table 1). Of the 513 patients with at least one measurement of ≥ 500 mg/dL, only 246 (48.0%) received at least one prescription of triglyceride-lowering drugs in the year following the last measurement.

In total, 3485 patients had an acute MI in 2015 (prevalence, 4.2%). Of these, only 288 (8.3%) received at least one prescription of triglyceride-lowering drugs in the year following this event.

4 Discussion

In this large epidemiological study, the prevalence and treatment of hypertriglyceridemia in the Rome area was evaluated using a database of anonymized clinical charts.

Overall, the prevalence of hypertriglyceridemia was lower than previously reported in Italy [1].

To identify patients with a formal diagnosis of hypertriglyceridemia not responding to first-line treatment, the present analysis focused on patients who had at least three measurements of triglyceride concentration of ≥ 200 mg/dL. Surprisingly, in this cohort, only approximately one in five had received appropriate treatment (fibrates in monotherapy or omega-3 fatty acids in monotherapy or in association with statins). In patients who had at least one measurement of triglyceride concentration of ≥ 500 mg/dL, the proportion of those who received treatment increased to approximately 50%. Nevertheless, treatment of hypertriglyceridemia in the Rome area appears to be neglected. This finding is further reinforced by the extremely low

Table 1 Prevalence of hypertriglyceridemia and the rate of treatment with lipid-lowering drugs in 2015 in the Rome area

Population	Number	Percentage (%)
Patients with one measurement of triglycerides concentration ≥ 200 mg/dL	2786/ 55,345	5.0
Patients with a diagnosis of hypertriglyceridemia confirmed with ≥ 3 measurements of triglycerides concentration ≥ 200 mg/dL	1653/ 55,345	3.0
Patients with ≥ 3 measurements of triglycerides concentration ≥ 200 mg/dL with at ≥ 1 prescription of triglyceride-lowering treatment in the following year	357/1653	21.6
Patients with ≥ 1 consecutive measurement of triglycerides concentration ≥ 500 mg/dL with ≥ 1 prescription of triglyceride-lowering treatment in the following year	246/513	48.0
Patients with myocardial infarction who received ≥ 1 prescription of triglyceride-lowering treatment in the year following this event	288/3485	8.3

proportion of patients (8%) with a prior history of acute MI who had received treatment for hypertriglyceridemia.

The results of this study show a pattern of inadequate treatment of hypertriglyceridemia in the Rome area. It is important that this pattern be addressed and corrected. Current guidelines issued by the European Society of Cardiology (ESC) state that the treatment of hypertriglyceridemia should be based on lifestyle modifications and therapy with statins with or without fibrates [4]. However, treatment with fibrates may be associated with increased non-cardiovascular mortality and the risk of adverse events [9]. In addition, statins have only a marginal effect on hypertriglyceridemia and, therefore, other therapeutic strategies are needed to effectively control this risk factor [8]. Omega-3 fatty acids, prescribed either as monotherapy or in combination with statins, have been shown to be effective and safe in the management of hypertriglyceridemia [10–12].

According to the Italian Medicines Agency (AIFA) [13], the treatment of hypertriglyceridemia is reimbursed in Italy only in patients with familial hypertriglyceridemia or with triglyceride concentrations of ≥ 500 mg/dL and concomitant renal insufficiency. However, it may be appropriate to treat all cases of hypertriglyceridemia because of the magnitude of its contribution to the risk of cardiovascular disease.

This study had several potential limitations. A diagnosis of hypertriglyceridemia was made on the basis of triglyceride values. However, epidemiological studies that rely on clinical charts can be affected by poor reporting and, indeed, a diagnosis of hypertriglyceridemia was directly reported by the patient in some clinical charts, which may explain why triglyceride values were absent in some cases. Furthermore, the diagnosis of hypertriglyceridemia may be missed because of concomitant diagnoses of conditions that can cause secondary hypertriglyceridemia (a diet rich in fats and carbohydrates, abuse of alcohol, diabetes, the metabolic syndrome, obesity) or of drugs potentially

affecting lipid metabolism. Nor does the diagnosis of hypertriglyceridemia necessarily require the prescribing of drugs, and a patient may independently purchase over-the-counter omega-3 fatty acids or other triglyceride-lowering nutraceuticals, such as berberine, or implement some or all of the lifestyle modifications recommended as the initial approach for managing dyslipidemias, such as adopting a diet low in saturated fats and carbohydrates and taking part in physical activity [4]. However, such interventions were not usually recorded.

Despite these limitations, the number of patients evaluated and the reliability of some of the variables analyzed (e.g., prescriptions) constitute the strengths of this study.

5 Conclusion

The impact of hypertriglyceridemia on the risk of cardiovascular events must not be underestimated. Treatment of this condition must be an integral part of an effective strategy for the prevention of cardiovascular events.

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Compliance with Ethical Standards

Conflicts of interest The authors declare that they have no conflict of interest.

Research Involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this study informed consent is not required.

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