Les patients hyperlipidémiques sont-ils sous-traités?

Étude de patients admis à l'hôpital pour un problème coronarien

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RÉSUMÉ

OBJECTIF Identifier les patients admis à l'hôpital pour un problème coronarien et estimer leur risque coronarien pré-admission, incluant le profil lipidique. En dépit des données et des nombreuses directives existantes, plusieurs patients hyperlipémiques sont sous-traités et n'atteignent pas les niveaux lipidiques cibles.

TYPE D'ÉTUDE Revue rétrospective de dossiers.

CONTEXTE Hôpital communautaire de soins actifs à Winnipeg, Manitoba.

PARTICIPANTS Un total de 153 patients admis à l'hôpital avec un diagnostic d'infarctus aigu du myocarde, d'angine instable ou de syndrome coronarien aigu.

MÉTHODE Pour chaque patient, on a calculé le risque de développer une maladie coronarienne dans un laps de 10 ans et déterminé son niveau de risque. Pour chacun, les niveaux du cholestérol des lipoprotéines de faible densité (LDL-C) a été mesuré et classé selon les normes canadiennes actuelles.

RÉSULTATS Les patients avaient en moyenne 67,6 ans; 60,8% étaient des hommes. Ceux de la classe à faible risque avaient un niveau moyen de LDL-C de 2,98 mmol/L (intervalle de confiance [IC] à 95%: 2,66-3,29) et ceux de la classe à risque modéré, un niveau moyen de LDL-C de 3,01 mmol/L (IC à 95%: 2,74-3,28), ces deux valeurs étant significativement inférieures aux niveaux cibles dans ces catégories de risque selon les normes canadiennes. Toutefois, ceux de la classe à risque très élevé avaient un niveau moyen de LDL-C de 2,53 mmol/L (IC à 95%; 2,35-2,71), ce qui dépasse la cible recommandée. Près de la moitié des patients (48,3%) de la classe à risque très élevé avaient des niveaux de LDL-C excédant les cibles. Un peu plus du tiers des patients de cette même catégorie prenait des hypolipidémiants.

CONCLUSION Les patients à très haut risque d'avoir un incident coronarien et qui vivent dans la communauté ne sont pas suffisamment traités pour atteindre les niveaux cibles de LDL-C. Ces résultats laissent croire qu'on peut prévenir la morbidité des patients et réduire le nombre d'hospitalisations pour des problèmes cardiovasculaires.

POINTS DE REPÈRE DU RÉDACTEUR

- Malgré les études à grande échelle démontrant que la réduction du cholestérol des lipoprotéines de faible densité (LDL-C) est associée à une réduction des incidents coronariens, les données actuelles suggèrent que plusieurs patients sont sous-traités et n'atteignent pas les niveau cibles recommandés par les directives de pratique.
- Cette étude voulait quantifier ce phénomène par une revue rétrospective de dossiers de patients admis pour certains problèmes cardiovasculaires à un hôpital communautaire de soins actifs.
- Près de la moitié des patients du groupe à risque très élevé avaient des niveaux de LDL-C dépassant les cibles recommandées.

Cet article a fait l'object d'une révision par des pairs.
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Are patients with hyperlipidemia undertreated?

Study of patients admitted to hospital with coronary events

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ABSTRACT

OBJECTIVE To identify patients admitted to hospital with coronary events and to estimate their pre-admission coronary risk, including their lipid levels. Despite the available data and numerous guidelines, evidence indicates that many patients with hyperlipidemia are undertreated and are not achieving target lipid levels.

DESIGN Retrospective chart review.

SETTING Acute care community hospital in Winnipeg, Man.

PARTICIPANTS A total of 153 patients who were diagnosed with acute myocardial infarction, unstable angina, or acute coronary syndrome upon admission.

METHOD Each patient's 10-year risk of developing coronary artery disease was calculated, and his or her risk status was established. Each patient's low-density lipoprotein cholesterol (LDL-C) levels were recorded and categorized based on current Canadian guidelines.

RESULTS Mean age of patients was 67.6 years; 60.8% were male. Patients in the low-risk category had a mean LDL-C level of 2.98 mmol/L (95% confidence interval [CI] 2.66 to 3.29), and patients in the moderate-risk category had a mean LDL-C level of 3.01 mmol/L (95% CI 2.74 to 3.28), both significantly lower ($P < .05$) than the LDL-C target levels for patients in those risk categories according to Canadian guidelines. The mean LDL-C level for patients in the very high-risk category, however, was 2.53 mmol/L (95% CI 2.35 to 2.71), above the recommended goal. Almost half the patients (48.3%) in the very high-risk category had LDL-C levels that exceeded the goal. Slightly more than 1 in 3 patients in the very high-risk category was reported to be taking lipid-lowering agents.

CONCLUSION Patients in the community who are at very high risk of having cardiovascular events are undertreated with respect to attaining LDL-C target levels. These findings point to an opportunity to prevent patient morbidity and reduce the number of hospitalizations for cardiovascular events.

EDITOR'S KEY POINTS

- Despite large-scale trials demonstrating that reductions in low-density lipoprotein cholesterol (LDL-C) levels are associated with a lower incidence of coronary events, evidence indicates that many patients are undertreated and are not achieving guideline-recommended target lipid levels.
- This study sought to quantify this phenomenon using a retrospective chart review of patients admitted to an acute care community hospital with certain cardiovascular events.
- Nearly half the patients stratified into the very high-risk group had LDL-C levels above the recommended target.

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Large-scale clinical trials have demonstrated that reducing serum low-density lipoprotein cholesterol (LDL-C) is associated with a lower incidence of coronary events[1-5] in both primary[3,4,6] and secondary[1,2,5] prevention situations. Virtually all trials demonstrated a decrease in coronary death and nonfatal myocardial infarction (MI), and some showed reductions in total mortality.[1,2,5] Other studies have found that aggressive lipid lowering reduces the number of ischemic events at about the same rate as coronary angioplasty does.[7]

Such findings have had a central role in formulating guidelines for treating dyslipidemias. The Canadian guidelines in use as we initiated this study were published in 2000.[8] In these guidelines, target LDL-C levels for patients deemed to be at low, moderate, high, or very high risk (as defined by their 10-year risk of coronary artery disease) were set at <5.0, <4.0, <3.0, and <2.5 mmol/L, respectively.

Based on Framingham data, risk-assessment tools have been developed to aid clinicians in assessing patients' risk for having cardiac events so that therapy can be tailored to risk status.[8,9] Evidence suggests, however, that many patients are undertreated and are not achieving guideline-recommended target lipid levels.[10,11] In this study, we set out to quantify this phenomenon in our community by means of a retrospective chart review of patients admitted to hospital with certain cardiovascular events.

METHOD

We conducted the study at an acute care community hospital in Winnipeg, Man. Before we started the study, we obtained approvals from the University of Manitoba Health Research Ethics Board and from the hospital. The Research Ethics Board waived the need for patient consent to access medical charts. We reviewed consecutive charts with admission diagnoses of acute MI, unstable angina, or acute coronary syndrome from the 2002-2003 and 2003-2004 fiscal years. Charts were excluded if lipid levels had not been measured within 24 hours of admission, if there was inadequate history to establish risk status, if patients were not expected to survive for 1 year due to noncardiac illness, or if patients were treated with only palliative measures.

We used a "treat to target" assessment tool for calculating the 10-year risk of coronary artery disease in nondiabetic people, as recommended by the Canadian Working Group on Hypercholesterolemia and Other Dyslipidemias.[8] Depending on the person's risk category, the tool directs users to the recommended target levels for LDL-C. We considered patients with diabetes as very high risk in keeping with the Canadian guidelines and based on the observation that diabetic patients without overt vascular disease appear to share the same risk as nondiabetic patients with documented vascular disease.[12]

Using a moderate effect size of 0.6 standard deviations[1,5,13] and an α set at .05 (1-tailed), power analysis revealed that we needed a sample size of 26 subjects per risk group (low, moderate, high, and very high) to achieve a power of 90%[14] in detecting a significant difference between actual and target LDL-C levels.

Pertinent demographic information was recorded along with the information necessary to complete a "treat to target" tool based on Framingham risk calculations. Each subject's risk points were added together to determine their 10-year risk of having coronary artery disease, allowing for risk categorization. Target LDL-C levels were recorded for each subject based on the 2000 Canadian guidelines.[8]

Our initial intent was to review charts until we had adequate data for analysis in each risk category. It became apparent, however, that very few patients fell into the high-risk category, and further culling of charts to locate sufficient patients in that category would have exceeded our resources. Hence, the 3 records in the high-risk group were not subjected to further analysis. Data were entered into an Excel 5.0 spreadsheet and analyzed using the Statistical Analysis software (SAS Institute).

Descriptive statistics were used to report numerical data on age, total cholesterol, high-density lipoprotein cholesterol, LDL-C, blood pressure (BP), calculated risk, and length of stay in hospital. Categorical data, such as primary diagnosis, smoking status, diabetes, and outcome, were described by relative frequencies expressed in percentages. Relative frequencies of risk categories and use of lipid-lowering agents before admission were calculated. One-sample *t* tests were used to determine the difference between actual and target LDL-C levels in each risk category. A 1-tailed α of .05 was used to determine statistical significance.

RESULTS

A total of 153 patient records were included in the analysis. Baseline characteristics and primary diagnoses

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are shown in **Table 1.** Results of risk stratification and LDL-C level findings stratified by risk category are shown in **Table 2.** Of the 153 patients evaluated, 21.6% were determined to be at low risk, 15.7% at moderate risk, and 60.8% at very high risk of coronary events. Mean LDL-C levels for the low- and moderate-risk groups were significantly lower than guideline target levels ($P<.001$, respectively). For the very high-risk group, however, although the mean LDL-C level was just above the target level ($P=.1$), nearly half the subjects (48.4%) had LDL-C levels above the recommended target level (**Table 3**).

Lipid-lowering agents had been prescribed to 24.8% of patients before admission. Percentages of patients prescribed lipid-lowering agents in each risk category are shown in **Table 2.** The mean LDL-C level for patients prescribed lipid-lowering agents (2.34 ±0.80) was significantly lower than that of patients not receiving these agents (2.86 ±0.88, $P=.002$). Use of lipid-lowering agents in very high-risk patients was also significantly associated with achieving target LDL-C levels. Among the very high-risk patients taking lipid-lowering agents, 62.5% achieved target LDL-C levels, while among those not taking these agents, only 45.9% had LDL-C levels in the target range ($P<.03$). Significantly more patients in the very high-risk group were taking lipid-lowering agents compared with patients in the low- or moderate-risk groups ($P=.012$, respectively). The mean LDL-C level in the very high-risk group was significantly lower than the mean LDL-C levels in the low-risk ($P<.01$) and moderate-risk ($P<.04$) groups.

The distribution of LDL-C levels of very high-risk patients whose levels were above target is shown in **Table 3.** Nearly half the patients (45/93, 48.4%) stratified into the very high-risk category had LDL-C levels above

Table 1. Patient and characteristics (N = 153): *A) Mean characteristics and laboratory values; B) Baseline conditions, primary diagnoses, and outcomes.*

A) CHARACTERISTIC	MEAN (STANDARD DEVIATION)
Age	67.6 (14.4)
Systolic blood pressure (mm Hg)	125.4 (23.3)
Diastolic blood pressure (mm Hg)	71.4 (11.5)
Total cholesterol (mmol/L)	4.65 (1.07)
High-density lipoprotein cholesterol (mmol/L)	1.13 (0.33)
Low-density lipoprotein cholesterol (mmol/L)	2.73 (0.88)
Length of stay in hospital (d)	7.1 (8.22)
B) CHARACTERISTIC	**N (%)**
Male	93 (60.8)
Smoker	39 (25.5)
Diabetes	41 (26.8)
Primary diagnosis	
• Myocardial infarction	111 (72.5)
• Acute coronary syndrome	28 (18.3)
• Unstable angina	14 (9.2)
Outcome	
• Death	7 (4.6)
• Discharged home	123 (80.4)
• Discharged to other acute care facility	22 (14.4)
• Other	1 (0.7)

Table 3. Low-density lipoprotein cholesterol levels over target among very high-risk patients: *N = 45.*

LDL-C LEVELS (MMOL/L) N (%)	NO. OF PATIENTS OVER TARGET
2.5-2. 7	8 (17.8)
2.7-2.9	5 (11.1)
2.9-3.1	6 (13.3)
3.1-3.3	8 (17.8)
3.3-3.5	4 (8.9)
3.5-3.7	5 (11.1)
3.7-3.9	1 (2.2)
3.9-4.1	3 (6.7)
>4.1	5 (11.1)

Table 2. Risk categories and low-density lipoprotein cholesterol (LDL-C) levels: *N = 153.*

RISK CATEGORY	TARGET LEVEL IN MMOL/L	N (%)	RECEIVING LIPID-LOWERING AGENTS N (%)	MEAN LDL-C LEVEL IN MMOL/L (95% CI)	*P* VALUE FOR MEAN LOWER THAN TARGET LEVEL	LDL-C HIGHER THAN TARGET LEVEL N (%)
Low	<5	33 (21.6)	3 (9.1)	2.98 (2.66-3.29)	<.001	0 (0.0)
Moderate	<4	24 (15.7)	3 (12.5)	3.01 (2.74-3.28)	.001	2 (8.3%)
High*		3 (2)				
Very high	<2.5	93 (60.8)	32 (34.4)†	2.53 (2.35-2.71)‡	.099	45 (48.4)

*No further analysis undertaken due to small numbers.
† $P=.005$ and 0.037 compared with low and moderate groups, respectively.
‡ $P=.012$ compared with low and moderate groups, respectively.

the target level of <2.5 mmol/L. Among the 7 people who died, 5 were in the very high-risk category.

DISCUSSION

Most of the patients presenting to our hospital with acute MI, acute coronary syndrome, or unstable angina were in the very high-risk category for coronary events. Almost half of them had LDL-C levels above the recommended level. Although more patients in this group were taking lipid-lowering agents than lower-risk patients were, two thirds of them (65.6%) were not taking them at all. Even among very high-risk patients taking lipid-lowering agents, 37.5% had LDL-C levels above target.

Unfortunately, these results demonstrate no improvement over levels published in earlier studies.[15,16] The Lipid Treatment Assessment Project[15] found that 63% of high-risk patients and 82% of patients with coronary artery disease (very high risk) failed to reach their target lipid levels. The Third National Health and Nutrition Examination Survey[16] found that, among survivors of MI or stroke with known hypercholesterolemia, 46% had poorly controlled lipid levels.

A 2003 Canadian survey of management of dyslipidemia in an academic family medicine clinic[10] identified a cohort of patients for whom target LDL-C levels were believed to be <2.5. Only 44% of patients with diabetes mellitus or documented coronary artery disease were prescribed lipid-lowering treatment, and only 48% achieved target LDL-C levels. In our survey, the proportion of very high-risk patients who attained target LDL-C levels was very similar (51.6%). Even fewer of our very high-risk patients (34.4%) were prescribed lipid-lowering treatment. Although the mean LDL-C level in very high-risk patients in our study was close to the target, almost half the patients' levels were higher than target: 26 patients (58%) had LDL-C levels at least 25% above target, and 9 (20%) had levels at least 50% above target. Most practitioners would consider these differences clinically significant in a very high-risk group.

Our data indicate that, despite their failure to achieve target LDL-C levels, very high-risk patients in the community were treated more aggressively than other patients were. The mean LDL-C level of patients in the very high-risk group was significantly lower than levels in the moderate- or low-risk groups (2.53 vs 2.98 and 3.01, respectively). In addition, 34.4% of very high-risk patients were taking lipid-lowering agents at the time of presentation, more than double the frequency in the other groups (9.1% in the low-risk category and 12.5% in the moderate-risk category), a statistically significant difference.

Many factors could be responsible for LDL-C levels being above target and for the low proportion of very high-risk patients taking lipid-lowering agents. Physicians might not know enough about or be in disagreement with guidelines, or they might not be motivated enough to follow the guidelines. Patient and environmental factors could include noncompliance, denial, concern regarding side effects, suspicion regarding risk-benefit ratios, use of herbal remedies, and cost. We did not explore these factors or determine their relative contributions.

Limitations

This study was a retrospective chart review in a hospital. Office records, including patients' lipid levels and the duration of lipid-lowering therapy were generally unavailable. Framingham-based risk assessment, although recommended by guidelines, is neither the only nor necessarily the best predictor of risk. Some risk factors, such as family history, were not taken into account.

Blood pressure at time of presentation to hospital might not represent "usual" BP. We attempted to correct this by using the first documented daytime BP on the second day of admission when patients were free of pain. Given patients' recent physical stress and emotional reactions, their BP might still have been higher than usual. On the other hand, many patients would have received new or increased doses of BP-lowering medications and would have been on bed rest, which might have led to underestimation of true BP. Most patients still fell into the very high-risk category, suggesting that the effect of any underestimation of BP on our results was negligible.

With the exception of the high-risk group, the sample size was adequate to determine statistical significance. We cannot comment further on the high-risk group, but this has no effect on the validity of our findings concerning the other groups. There were only 24 patients in the moderate-risk group when we stopped collecting data, but the difference between their mean LDL-C level and the target level was highly statistically significant; finding 2 more such patients would have taxed our resources with no chance of having a material effect on this finding.

Patients in previously published surveys[7,15] have been identified from pools of stable outpatients. Our study adds to the current literature by identifying patients at a different point in the spectrum of hyperlipidemia and coronary artery disease: on admission to hospital with coronary events, at which time we were able to estimate their risk of such events.

Conclusion

Failure to achieve target lipid levels represents a possible missed opportunity to prevent coronary events and hospital admissions. Our results clearly mirror the results of other surveys[10,11,15,17] and suggest that patients in our community were undertreated with respect to reaching LDL-C target levels. Our findings indicate an opportunity to prevent patient morbidity and hospitalizations related to vascular events by influencing both physicians

and patients. While new Canadian guidelines were published in late 2003,[18] and more recently in 2006[19] (recommending more aggressive lipid lowering), our study offers a unique glimpse into the "state of affairs" of treating hyperlipidemia at the end of the 2000 guidelines' lifespan. These findings also suggest that we have much work to do to conform to current recommendations.

Contributors

Dr Lipson *conceived and designed the study and wrote this paper.* **Dr Fallis** *refined the study design, supervised the collection of data, and contributed to writing this paper.* **Drs Lipson** *and* **Fallis** *take responsibility for the integrity of the paper as a whole.* **Dr Wang** *was involved in study design and was responsible for the power calculations and determination of sample sizes. He also supervised* **Ms Yi** *and contributed to writing this paper.* **Ms Yi** *did most of the data analysis.*

Competing interests

None declared

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