Original Article

Landscape of Lipid Management Following an Acute Coronary Syndrome Event: Survey of Canadian Specialists

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ABSTRACT

Background: Following the occurrence of an acute coronary syndrome (ACS), patients are at high risk for subsequent cardiovascular events. Therapies to lower the level of low-density lipoprotein (LDL) cholesterol remain a pillar in secondary prevention approaches following ACS. Significant variability remains in the application of therapies to lower cholesterol level in clinical practice.

Methods: A cross-sectional, online survey was conducted of 200 cardiovascular and lipid specialists across Canada who routinely care for patients following the occurrence of ACSs. The survey consisted of 50 multiple-choice questions with opportunities for free-text entry exploring knowledge of lipid guidelines and recent clinical trials, and in-hospital and outpatient management of lipids and familial hypercholesterolemia.

RÉSUMÉ

Contexte : Après un syndrome coronarien aigu (SCA), le risque qu'un autre événement cardiovasculaire survienne est élevé. Les traitements visant à réduire le taux de cholestérol des lipoprotéines de basse densité (C-LDL) demeurent l'un des piliers de la prévention secondaire après un SCA. Dans la pratique clinique, l'utilisation de ces traitements varie considérablement d'un praticien à l'autre.

Méthodologie : Nous avons mené une enquête transversale en ligne auprès de 200 spécialistes de la santé cardiovasculaire et des lipides de partout au Canada, qui traitent régulièrement des patients ayant subi un SCA. L'enquête comprenait 50 questions à choix multiples; les participants pouvaient aussi donner des réponses détaillées permettant d'évaluer leurs connaissances des lignes directrices en matière de maîtrise des lipides et des essais cliniques récents, ainsi

Every year, ~72,000 Canadians are hospitalized with an acute coronary syndrome (ACS).¹ Despite advances in early interventions and access to care, 10%–20% of individuals will go on to experience a second ACS event within the first 2 years following their initial event.^{2,3} In patients with familial hypercholesterolemia (FH), the risk of a second ACS event is markedly higher.⁴ As a result, following the occurrence of an ACS, there is significant focus on preventative therapies, particularly the lowering of low-density lipoprotein (LDL) cholesterol level. Evidence from large, randomized clinical

trials has demonstrated that high-intensity statins, ezetimibe, and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are effective in reducing secondary cardiovascular events,^{5–8} as reflected in the recommendations of national and international guidelines for lipid management.^{9–11} These guidelines unanimously support an LDL cholesterol level target of < 1.8 mmol/L in high-risk populations, such as those who have an ACS. Despite these guideline recommendations, it remains challenging to achieve these targets, with recent estimates suggesting that only ~50% of high-risk Canadian patients have an LDL cholesterol level at or below a target of 2.0 mmol/L.¹² The European Society of Cardiology guidelines also recommend that in very high-risk patients, an LDL cholesterol target of < 1.4 mmol/L be considered.¹⁰ With more-aggressive reductions in LDL cholesterol being recommended, the proportion of patients meeting these targets can be expected to decrease.

It is valuable, therefore, to better understand patterns of practice with respect to lipid assessment and use of therapies

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Ethics Statement: The research reported herein has adhered to relevant ethical standards.

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See page 630 for disclosure information.

Results: A total of 67.5% (n = 135) of participants stated that a lipid panel would routinely be obtained during the first 24 hours of an admission for an ACS, and 68.5% (n = 137) stated that their hospitals had standing orders for statin initiation at ACS presentation. In high-risk patients, the majority (75.5%; n = 151) of participants indicated that they target an LDL cholesterol level of <1.8 mmol/L. However, a subset (22%; n = 44) would target lower LDL cholesterol levels ranging from 0.5 to 1.7 mmol/L. Only 32.0% (n = 64) of participants stated that >70% of their ACS patients were at or below guideline-recommended LDL cholesterol levels. Respondents generally underappreciated the prevalence of familial hypercholesterolemia in both the general population and ACS patients.

Conclusions: There is significant variation in practice patterns involving therapies to lower LDL cholesterol level in the post-ACS onset period. To improve management of lipids in this high-risk population, changes to institutional policies, shared responsibility of lipid management across multiple disciplines, and physician education are required.

to lower LDL cholesterol level by specialists managing patients who have had a recent ACS event.

Methods

Questionnaire development

In collaboration with the Canadian Collaborative Research Network (CCRN), the Guideline Application in ACS Patients steering committee (R.W., J.G., R.H., M.G.) created an online questionnaire to explore the current state of specialist lipid management in ACS patients across Canada. The CCRN is a not-for-profit organization that develops learning programs for physicians across multiple specialties. The steering committee is made up of a group of cardiologists with an interest in quality improvement initiatives to promote guideline-directed therapy in the ACS setting. The questionnaire ([Supplemental Appendix S1](#)) was composed of 50 multiple-choice questions, free-text questions, and clinical cases. The survey questions were distributed to 7 cardiovascular and lipid specialists to assess for face and content validity, with feedback incorporated into the final survey. Reliability was not assessed.

Participants

In June 2019, the CCRN distributed the survey electronically, through their membership list, using SurveyMonkey, to cardiologists, internal medicine specialists, and lipid specialists who routinely treat ACS patients. The membership list consists of 1551 specialists who have indicated either cardiology or dyslipidemia as their primary area of practice. The physicians have joined the CCRN or opted in after the completion of the CCRN continuing

que de la prise en charge de la lipidémie et de l'hypercholestérolémie familiale en contexte hospitalier et ambulatoire.

Résultats : Au total, 67,5 % (n = 135) des participants ont déclaré demander systématiquement un bilan lipidique complet dans les 24 heures suivant l'admission d'un patient en raison d'un SCA, et 68,5 % (n = 137) des participants ont dit que la norme dans leur hôpital était d'instaurer un traitement par statine chez tous les patients ayant subi un SCA. Dans le cas des patients présentant un risque élevé, la majorité des participants (75,5 %, n = 151) ont indiqué qu'ils ciblaient un taux de C-LDL de moins de 1,8 mmol/l. Une partie de ces répondants (22 %, n = 44) ont dit cibler un taux de C-LDL encore plus bas, soit de 0,5 à 1,7 mmol/l. Seulement 32,0 % (n = 64) des répondants ont déclaré que plus de 70 % de leurs patients ayant subi un SCA avaient un taux de C-LDL à la limite ou en deçà du taux recommandé dans les lignes directrices. Les répondants ont en général sous-estimé la prévalence de l'hypercholestérolémie familiale dans la population générale et chez les patients ayant subi un SCA.

Conclusions : Les pratiques varient considérablement d'un praticien à l'autre en ce qui concerne les traitements visant à diminuer le taux de C-LDL après la survenue d'un SCA. Afin d'améliorer la prise en charge de la lipidémie dans cette population exposée à un risque élevé, il conviendrait de revoir les politiques des établissements, de répartir la responsabilité de la prise en charge de la lipidémie entre les intervenants de différentes disciplines et de mieux informer les médecins.

medical education courses. The first 200 responses were collected, after which the survey was closed. Participants were offered a \$125 stipend for their participation in the survey.

Statistical analysis

All analysis was conducted using SPSS (version 26; IBM, Chicago, IL). Results are reported in frequencies and percentages. Averages are reported as means and standard deviations.

Results

Participant demographics

A total of 200 participants responded to the survey (response rate = 12.9%); demographics of respondents are shown in [Table 1](#). Participants treated patients with ACS on a regular basis. In the preceding 3 months, 72% (n = 144) had treated more than 5 patients with recent ACS in their outpatient practice. Participants practiced predominantly (n = 175; 87.5%) according to the 2016 Canadian Cardiovascular Society Lipid Guidelines,⁹ compared to 9% (n = 18) who used the 2018 American College of Cardiology/American Heart Association guidelines,¹¹ and 2% (n = 4) who used the 2019 European Society for Cardiology/European Atherosclerosis Society guidelines.¹⁰ Three participants (1.5%) stated that they used a combination of these guidelines.

Assessment of knowledge of the 2016 Canadian Cardiovascular Society guidelines

Regarding lipid-profile determination, 57% (n = 114) correctly identified that a non-fasting lipid profile is an

Table 1. Survey respondent demographics

Respondent characteristics	n (%)
Specialty	
Internal medicine	47 (23.5)
Lipidology	15 (7.5)
Cardiology	138 (69.0)
General	85 (42.5)
Interventional	19 (9.5)
Imaging	17 (8.5)
Heart failure	9 (4.5)
Electrophysiology	7 (3.5)
Cardiac rehabilitation	1 (0.5)
Province of practice	
Alberta	10 (5.0)
British Columbia	26 (13.0)
Manitoba	6 (3.0)
New Brunswick	6 (3.0)
Newfoundland and Labrador	1 (0.5)
Nova Scotia	4 (2.0)
Ontario	105 (52.5)
Quebec	39 (19.5)
Saskatchewan	3 (1.5)
Practice location (population)	
Metropolitan (> 500,000)	109 (54.5)
Urban (> 100,000)	70 (35.0)
Rural (< 100,000)	21 (10.5)
Practice setting (multiple answers accepted)	
Tertiary hospital	91 (45.5)
Outpatient practice	90 (45.0)
Community hospital	79 (39.5)
CCU	123 (61.5)
Hospital with a CCU	180 (90.0)
PCI-capable hospital	133 (66.5)
Years in practice	
0-5	26 (13.0)
6-10	28 (14.0)
11-15	32 (16.0)
16-25	56 (28.0)
≥ 26	58 (29.0)

CCU, coronary care unit; PCI, percutaneous coronary intervention.

acceptable test, with 25.5% (n = 51) believing that a fasting lipid profile should be undertaken for all patients, and 11% (n = 22) believing that a fasting lipid profile should be undertaken in patients already receiving lipid-lowering treatment. In addition, 47.5% (n = 95) also correctly identified that a fasting lipid profile should be undertaken if the triglyceride level is known or suspected to be > 4.5 mmol/L.

In patients with stable coronary artery disease, 93.0% and 64.5% (n = 186 and 129) identified that an LDL cholesterol level consistently < 2.0 mmol, and a > 50% reduction in LDL cholesterol, are recommended targets, respectively, per guidelines. Participants were less likely to identify that apolipoprotein (apo) B < 0.8 g/L (49.0%; n = 98) and a non-high-density lipoprotein cholesterol level < 2.6 mmol/L (46.0%; n = 92) are alternative targets. For patients with an ACS, 96.5% (n = 193) identified an LDL cholesterol level of < 1.8 mmol or a > 50% reduction in LDL cholesterol as guideline-endorsed targets.

Clinical trial awareness

Participants were asked to describe their awareness of the design and results of recent major clinical trials in lipid management. A total of 60%-75% of respondents were moderately or extremely aware of the **Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-**

IT) investigating the use of ezetimibe in addition to statin therapy following occurrence of an ACS (75.8%; n = 150),⁵ the **Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk (FOURIER)** trial investigating the use of evolocumab in addition to statin therapy in patients with atherosclerotic cardiovascular disease (62.3%; n = 124),⁷ and the **Odyssey Outcomes** trial investigating the use of alirocumab in addition to statin therapy following occurrence of an ACS (60.8%; n = 121).⁸ However, only a quarter of respondents were aware of the **Studies of PCSK9 Inhibition and the Reduction of Vascular Events (SPIRE) 1 and 2** trials investigating bococizumab in high-risk cardiovascular patients (26.7%; n = 53 for SPIRE 1 and 25.8%; n = 51 for SPIRE 2).¹³

Lipid-lowering targets and therapies

Participants were asked to identify their LDL cholesterol targets for very high-risk patients (ie, those with multiple events, polyvascular disease, and cardiovascular disease in the presence of diabetes or chronic kidney disease) in comparison to those with stable atherosclerotic cardiovascular disease. The majority (75.5%; n = 151) identified a target of < 1.8 mmol/L; however, 22.0% (n = 44) used more-aggressive targets, ranging from < 1.8 to < 1.0 mmol/L. A total of 38.5% (n = 77) demonstrated some degree of concern regarding the safety (muscle pain, haemorrhagic stroke, and death due to cancer) of extremely low on-treatment LDL cholesterol levels (< 1.0 mmol/L).

The majority (65%; n = 130) reported that statin intolerance was exhibited in less than 20% of their patients, although one-third felt that statin intolerance occurred in more than 20%-40% of their patients. Participants demonstrated a wide range of experiences prescribing PCSK9 inhibitors, with 13% (n = 26) having never prescribed a PCSK9 inhibitor, and 23.0% (n = 46) having prescribed them to > 25 patients.

In-hospital lipid management

The majority (67.5%; n = 135) of participants stated that lipid levels are routinely measured within the first 24 hours of ACS presentation. Among participants, 68.5% (n = 137) stated that there are standing hospital orders in place to initiate statin therapy at the time of ACS presentation. The most frequent standing orders were for atorvastatin 80 mg daily (75.9%; n = 104) and rosuvastatin 40 mg daily (29.3%; n = 40). If patients were already on a low-dose statin at the time of ACS presentation, 71.5% (n = 143) stated that the dose would be routinely intensified. If already on high-intensity statin therapy, 80.0% (n = 160) recommended adding ezetimibe during ACS hospitalization.

Postdischarge lipid management

Following discharge from an ACS admission, 67.5% (n = 135) recommended that the initial follow-up visit should occur with the discharging cardiologist; 30.0% (n = 60) indicated the primary care physician; and 15.5% (n = 31) recommended a general internist. The majority (64.5%; n = 129) indicated that follow-up should occur between 1 and 3 months postdischarge; and 23.5% (n = 47) indicated that it should occur sooner (< 1 month postdischarge).

Table 2. Comparison of guideline recommendations for lipid management following an acute coronary syndrome event

	CCS Guidelines 2016	ESC/EAS Guidelines 2019	AHA/ACC Guidelines 2018
When to initially measure		As soon as possible after hospital admission	
LDL-C target, mmol/L	< 1.8	< 1.4 < 1.0 in those with recurrent event within 2 y on maximally tolerated statin therapy	< 1.8
When to remeasure		4-6 wk	
Add on therapies	Ezetimibe to those not at target on maximal statin dose, or statin intolerant; PCSK9 on those not at target on statin/ezetimibe		

ACC, American College of Cardiology; AHA, American Heart Association; CCS, Canadian Cardiovascular Society; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9.

Most (78.0%; $n = 156$) participants stated that during the first follow-up visit, on-treatment LDL cholesterol levels are routinely available; however, only 43.0% ($n = 86$) personally ordered a lipid panel prior to the follow-up visit. Only a minority of specialists perceived that >70% of their patients were achieving LDL cholesterol level targets in clinical practice (41.5%; $n = 83$ for stable atherosclerotic cardiovascular disease and 32.0%; $n = 64$ for ACS). Most participants (94.0%; $n = 188$) stated that there was a cardiac rehabilitation program in their region, but only 55.3% ($n = 104$) of these programs routinely adjust lipid therapies.

Case Study #1

You are seeing a 34-year-old male truck driver. His cardiac risk factors include regular smoking. He has a strong family history of premature coronary artery disease (father had a myocardial infarction in his 5th decade). He presents with an inferior ST-elevation myocardial infarction treated with primary percutaneous intervention with 2 drug-eluting stents placed in the left anterior descending coronary artery, and one stent placed in the posterior interventricular artery. On examination, he was found to have a grade-3 systolic murmur at the left sternal border. He is discharged on atorvastatin 80 mg daily in addition to aspirin, ticagrelor, ramipril, and metoprolol. A repeat lipid panel 8 weeks following discharge demonstrated a total cholesterol of 6.2 mmol/L, LDL cholesterol of 3.8 mmol/L, HDL cholesterol of 1.0 mmol/L, and triglycerides of 1.3 mmol/L. What would you do next?

Case discussion and FH

Participants were asked what they believed to be the most likely cause of this patient's murmur, which may be associated with severe FH. Only 24.0% ($n = 48$) correctly identified the etiology of the murmur as aortic stenosis. The remainder indicated acute ischemic mitral regurgitation (56.0%; $n = 112$), ventricular septal defect (11.5%; $n = 23$), and an innocent flow murmur (8.5%; $n = 17$). When asked to postulate what this patient's statin-naïve LDL cholesterol level may have been, 9.5% ($n = 19$) indicated 4.5 mmol/L, 51.5% ($n = 103$) indicated 6.6 mmol/L, and 28.0% ($n = 56$) correctly indicated 8.1 mmol/L. The majority (88.0%; $n = 176$) correctly agreed that the most likely diagnosis in this

patient was FH, and 87.5% ($n = 175$) indicated that adding a PCSK9 inhibitor was the appropriate therapy to pursue next.

Participants generally underestimated the prevalence of FH in the general population, with 28.0% ($n = 56$) correctly indicating 1:250, and 59.5% ($n = 119$) underestimating the prevalence. In the ACS population, 39.5% ($n = 79$) of participants correctly identified an FH prevalence of 1:100, but only 26.0% ($n = 52$) underestimated the prevalence. When asked how a diagnosis of FH is made, responses varied and most commonly included the following: according to Canadian Cardiovascular Society FH criteria (33.5%; $n = 67$); per Simon Broome Diagnostic Criteria (27.0%; $n = 54$); according to LDL cholesterol level alone (11.5%; $n = 23$); and per genetic testing (3.0%; $n = 6$).

Discussion

This study represents the first survey of cardiovascular and lipid specialists across Canada regarding lipid management in ACS patients. Akin to the experiences of our participants, many studies have demonstrated that achieving guideline-directed LDL cholesterol level targets in this population remains challenging. Although national and international guidelines provide lipid level targets following an ACS, there are limited recommendations for how to best achieve these targets⁹⁻¹¹ (Table 2). Our study highlights the fact that there are multiple opportunities that may improve this situation, including institutional policies, shared responsibility of lipid management, physician education, and improved awareness of FH (Fig. 1).

Institutional policies

Our study suggests that there are gaps in institutional policies that promote targeted lipid management. Only two-thirds of our respondents stated that ACS patients received routine lipid measurement within 24 hours of hospitalization. Similarly, observational studies have demonstrated that lipid levels were obtained in only 57%-73% of patients.¹⁴⁻¹⁷ To expedite appropriate escalation of lipid management (increased statin dose or addition of ezetimibe), we advocate use of an automated process, such as order sets or clinical reminders, to ensure that ACS patients have lipid evaluation within the first 24 hours of admission. In addition, the proportion of ACS patients undergoing lipid evaluation within the first 24 hours after hospital admission, and the proportion of ACS patients discharged on high-intensity statin therapy, should be used as metrics for quality of care.

Figure 1. Opportunities for addressing care gaps. ACS, acute coronary syndrome.

Shared responsibility

Following occurrence of an ACS, patients may have a plethora of clinical encounters with their primary care physician, cardiologist or internist, cardiac rehabilitation program, and pharmacist. With each of these encounters, there are opportunities to improve lipid management, but whether providers harness them is another issue. With multiple providers, there is the possibility of a loss of sense of responsibility over lipid management, as evidenced in our study, in which only 43% of respondents indicated that they would personally order lipid measurements at follow-up after ACS discharge. Clear communication between discharging physicians and primary care providers (and treating specialists) regarding when to repeat lipid measurements, when to escalate therapies, and which targets to achieve may help improve this situation. Cardiac rehabilitation and pharmacist-led programs have also demonstrated the ability to improve the management of dyslipidemia in this population.¹⁸⁻²⁴ Empowering nonphysician members of the multidisciplinary team required to care for ACS patients following discharge is crucial to tackling the challenges, with optimised lipid management.

Continuing education

There is a continuous stream of new evidence to guide the management of lipids in patients following an ACS event. These new findings need to be coupled with local and national initiatives to disseminate the information targeting specialists, primary care practitioners, and patients themselves. Our study identifies several potential targets for educational initiatives, including the following: when to measure lipids following an ACS event; the recommendation for non-fasting lipid panels; LDL cholesterol targets in various populations; how to deal with statin intolerance; recognition of FH in the ACS population; and when and how to prescribe PCSK9 inhibitors.

The case study included in our survey alongside the responses of our participants highlights the fact that even among cardiovascular specialists there remain educational opportunities surrounding FH. FH is profoundly underdiagnosed, with an estimated 90% of cases in Canada going undiagnosed.²⁵ The prevalence of FH in the general population is most commonly estimated to be 1:250, but it is

significantly higher among the ACS population, with a prevalence of 1:100.^{26,27} This places cardiovascular specialists who treat patients with ACS in a unique position to identify this high-risk population. Recently, a simplified Canadian FH definition has been proposed, with a “definite” diagnosis of FH based on: (i) LDL cholesterol level > 8.5 mmol/L; or (ii) LDL cholesterol level $\geq$ 5.0 mmol/L in patients aged $\geq$ 40 years, $\geq$ 4.5 mmol/L in patients aged 18-39 years, and $\geq$ 4.0 mmol/L in patients aged < 18 years. The LDL cholesterol cutoffs in the second criterion must be accompanied by one of the following: tendon xanthomas; genetic testing with mutation in the low-density lipoprotein receptor (LDLR), apolipoprotein B (APOB), or PCSK9 genes; or first-degree relative with positive genetic testing.²⁸ Baseline LDL cholesterol levels are frequently confounded by the concurrent use of statins in patients admitted with ACS. Understanding that lipid-lowering therapies create a predictable reduction in LDL cholesterol level may assist physicians in making the diagnosis of FH.²⁹ For example, in a patient on atorvastatin 80 mg daily, dividing the LDL cholesterol value on therapy by 0.49 will provide an estimate of their off-therapy LDL cholesterol level. A simple, easy-to-use tool based on these principles is available using the Cardio Risk Calculator (Cardiovascular Imaging Research Core Lab, University of British Columbia, Canada). Once patients are diagnosed with FH, there should be a strong index of suspicion for concomitant valvular disease, as even young patients have a significantly higher prevalence of subclinical aortic stenosis.³⁰

Limitations

Numerous limitations must be taken into account in interpreting the results of our survey, including the relatively small sample size and the geographical distribution of respondents, which limit the generalizability of our results. Also, the CCRN membership list may not be fully reflective of cardiologists, internal medicine specialists, and lipidologists across the country. In addition, our survey assessed respondent perceptions rather than objective endpoints. For example, although our survey demonstrated that only ~30% of respondents perceived that >70% of their ACS patients are at their LDL target level, objectively this was not demonstrated.

The challenge of managing lipids in patients following an ACS event is multifactorial, and as a result, any initiative to combat this must be multifaceted and harness the power of the multidisciplinary team.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjopen.ca/> and at <https://doi.org/10.1016/j.cjco.2020.08.009>.