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Special Article

Secondary Prevention Beyond Hospital Discharge for Acute Coronary Syndrome: Evidence-Based Recommendations

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ABSTRACT

In the past 3 decades, a better understanding of the pathophysiology of cardiovascular disease has resulted in innovations in the treatment and prevention of its clinical manifestations such as death, myocardial infarction, or stroke. After an acute coronary syndrome there are short- and long-term risks of subsequent cardiovascular events. This leads to opportunities to initiate strategies to reduce complications resulting from myocardial injury (cardiac protection) and to prevent recurrent acute coronary events (vascular protection). The results from clinical trials inform best practice and guidelines for patient management. Despite clear and consistent guidelines, an important number of patients are not receiving these treatments. Moreover, many others do not receive treatment that follows the strategy proven in the clinical trial and this is associated with a significant loss of opportunities to improve outcomes. The Canadian Heart Research Centre has therefore assembled a panel of experts to provide a review of available data and distill it to specific evidence-based recommendations that can be used

RÉSUMÉ

Au cours des trois dernières décennies, une meilleure compréhension des mécanismes physiopathologiques des maladies cardiovasculaires a permis toute une série d'innovations en matière de traitement et de prévention des manifestations cliniques de la maladie comme le décès, l'infarctus du myocarde ou l'accident vasculaire cérébral. Suivant un syndrome coronarien aigu, le patient court le risque, tant à court qu'à long terme, de subir d'autres événements cardiovasculaires. C'est donc l'occasion d'appliquer des stratégies visant à réduire les complications ultérieures liées aux lésions du myocarde (protection cardiaque) et à prévenir la survenue d'autres événements coronariens aigus (protection vasculaire). Les résultats des études cliniques dictent les meilleures pratiques cliniques et les lignes directrices de prise en charge des patients. Cependant, en dépit de l'existence de lignes directrices claires, un grand nombre de patients ne reçoivent toujours pas un traitement approprié et bien d'autres encore ne sont pas traités conformément aux stratégies éprouvées, ce qui signifie que l'on perd

Management of cardiovascular (CV) disease (CVD) involves more physicians and patients than any other disease. The profound effect of CVD on our civilization over the past 200 years has led to an unparalleled explosion of new drug development and clinical trials in its treatment and in its prevention. As a result of successful risk factor management (especially smoking cessation) and treatment, the age-adjusted mortality from CVD has been reduced almost 50% over the past 30 years.[1,2] Secondary prevention in patients with established CVD provides an opportunity to have a large effect in reducing risk in patients at an especially high risk of recurrent CVD events.

An acute coronary syndrome (ACS) is a pivotal event in the natural history of atherosclerosis. It is frequently the first presentation of coronary artery disease and the event that identifies the need for secondary prevention strategies. After an ACS the hazard of recurrent fatal and nonfatal ischemic events remains substantially increased for at least the next 6-12 months. Thus, effective management of patients during this high-risk period with secondary prevention provides an important opportunity to improve life expectancy, and enhance the quality of life. ACS guidelines from the American College of Cardiology (ACC)/American Heart Association

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by specialists and primary care physicians as a platform for secondary prevention. The therapeutic recommendations are conveniently divided into vascular protection (dual antiplatelet therapy, lipid-lowering, and renin angiotensin system inhibition) which should be considered in all patients; cardiac protection (addition of β-blocker therapy) in patients with left ventricular dysfunction including consideration for management of heart failure; and continuing management of risk factors and comorbid conditions on the basis of the specific patient profile. These recommendations are intended as a decision support tool and a quick reference for Canadian physicians.

actuellement beaucoup d'occasions d'améliorer les issues thérapeutiques de tels patients. C'est pourquoi le Centre canadien de recherche en cardiologie a décidé de créer un comité d'experts qui a passé en revue l'ensemble des données probantes disponibles afin d'établir une série de recommandations portant spécifiquement sur la prévention secondaire à l'usage des spécialistes et des médecins de première ligne. Pour plus de commodité, les recommandations ont été divisées en deux grandes catégories, soit 1) la protection vasculaire (traitement antiplaquettaire double, traitement hypolipidémiant et inhibition du système rénine-angiotensine) qui devrait être envisagée pour tous les patients et 2) la protection cardiaque (ajout d'un β-bloquant) pour les patients qui présentent une dysfonction ventriculaire gauche de même que pour la prise en charge de l'insuffisance cardiaque. À ces stratégies de traitement viendront s'ajouter une gestion continue des facteurs de risque et des comorbidités en fonction des besoins particuliers de chaque patient. Ces recommandations se veulent un outil décisionnel et un guide référence rapide à l'intention de tous les médecins canadiens.

(AHA)[3] have focused mostly on immediate in-hospital-based therapy, with less emphasis on recommendations after hospital discharge. Recommendations that are accessible and relevant for all physicians who manage patients with a recent ACS, if applied, could improve patient outcomes.

Current evidence indicates an improved survival when patients are treated with optimal secondary prevention strategies, and improved application has the potential to benefit Canadian patients.[4] The importance of optimal (evidence-based) dosing of specific agents after an ACS and the need for up-titration after discharge to achieve optimal doses has been identified as a key performance measure.[5] Unfortunately, despite recommendations from multiple national guidelines, secondary prevention measures are often not initiated at the time of the patient's admission or discharge from hospital after the ACS event.[6] Therefore, the Canadian Heart Research Centre, a nonprofit academic research organization, has undertaken the development of these recommendations by assembling an ad hoc panel of experts to provide specific evidence-based suggestions using specific agents and dosing that have been shown to be of benefit for secondary prevention after hospital discharge.

The definition of evidence-based treatment is important to define and inform optimal management. For the purposes of these practical and easy to use therapeutic suggestions we defined evidence-based therapy as that supported by a peer-reviewed publication of a properly conducted clinical trial showing clear clinical and statistical benefit that outweighs its side effects compared with placebo or available therapies. In that regard, our approach is similar to the US Food and Drug Administration guidance[7] for CV safety, whereby CV effect has to be studied beyond target measures such as blood pressure (BP) or glycemic control.

Consensus-based recommendations were used whenever clinical trial data were not specific or definitive; wherever possible published recommendations were relied on to avoid duplication or confusion. Where possible, specific drug and dose used in the pivotal trials were cited to produce more specific recommendations, which are preferred by many among the target audience for this document.

Recurrent Ischemic Events After an ACS

Clinical trials with current management strategies show that patients with a recent ACS continue to have a high event rate during the first weeks after the index admission. In the **S**uperior **Y**ield of the **N**ew Strategy of **E**noxaparin, **R**evascularisation and **Gly**coprotein IIb/IIIa Inhibitors (SYNERGY) trial[8] of patients with non-ST segment elevation (NSTE) ACS, 8% of patients died in the first year; almost half of these deaths occurred in the first 60 days. Death or recurrent myocardial infarction (MI) occurred in 18%, with 75% of such events occurring in the first 30 days. Patients with diabetes are at an especially high risk, with recurrent early and later ischemic events, resulting in a 1-year mortality approximately twice that of individuals without diabetes.[9]

The **G**lobal **R**egistry of **A**cute **C**oronary **E**vents (GRACE)[10] showed that during a 5-year follow-up of patients with ACS from the United Kingdom and Belgium, 19.8% died, 9.3% had a recurrent MI, 7.7% had a stroke, and 31% of patients were readmitted to hospital. Less than one-fifth of deaths occurred during the initial hospitalization. CV mortality occurred at similar rates in patients who presented with NSTE ACS (22%) as with ST segment elevation MI (19%). In the GRACE 2-year follow-up project, which included patients from Canada, important later adverse consequences, including frequent morbidity and mortality were observed. This was despite coronary procedures and the use of evidence-based therapies in a substantial proportion of patients.[11] A recently reported experience from Swedish national registries[12] also describes a high proportion of recurrent CV events after discharge from hospital for a first MI. Risk for nonfatal MI, nonfatal stroke, or CV death was 18.3% during the first 365 days after the index MI; for patients without an event during the first year, the subsequent composite end point risk was 20% in the next 36 months.

Recurrent acute coronary events are as likely to be a consequence of activation of a new coronary atherosclerotic plaque as a result from reocclusion of the original culprit lesion. The **P**roviding **R**egional **O**bservations to **S**tudy **P**redictors of **E**vents in the **C**oronary **T**ree (PROSPECT) study[13] observed 697 subjects over 3.4 years after an ACS. One-fifth