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2018 Clinical Practice Guidelines

Management of Acute Coronary Syndromes

Diabetes Canada Clinical Practice Guidelines Expert Committee

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KEY MESSAGES

- Over the past 20 years, the rates of acute myocardial infarction in people with diabetes has decreased substantially. However, the burden of disease remains high because of the increased prevalence of diabetes.
- Diabetes and hyperglycemia are independent predictors of increased short- and long-term mortality, recurrent myocardial infarction, and the development of heart failure in patients with acute myocardial infarction.
- People with an acute myocardial infarction and hyperglycemia (random blood glucose >11.0 mmol/L) may receive antihyperglycemic therapy to maintain blood glucose levels between 7.0 to 10.0 mmol/L.
- People with diabetes are less likely to receive recommended treatment, such as an early invasive strategy and revascularization, reperfusion therapy, beta blockers or dual antiplatelet therapy than people without diabetes. Efforts should be directed at promoting adherence to existing proven therapies in the high-risk person with myocardial infarction and diabetes.

KEY MESSAGES FOR PEOPLE WITH DIABETES

- A heart attack can manifest as chest discomfort or crushing pain; or as pain in the arms, back, neck, jaw and, even, the stomach. Shortness of breath, cold sweat, nausea and lightheadedness may also occur.
- If you are experiencing symptoms of a heart attack, you should seek medical help immediately. The faster treatment is started, the better.

Introduction

Diabetes (together with lipid abnormalities, smoking and hypertension) is one of the top 4 independent risk factors for myocardial infarction (MI) (1). Today, approximately 15% to 35% of people admitted with an acute coronary syndrome (ACS) have known diabetes (2), and as many as a further 15% have undiagnosed diabetes (3). Between 1990 and 2010, there was a 67.8% reduction of the rates of acute MI in people with diabetes, compared to a 32% reduction in individuals without diabetes (4). However, as a result of the substantial increase in the prevalence of diabetes over this period, the public health burden of MI in people with diabetes continues to rise.

Compared to individuals without diabetes, people with diabetes have:

- A 3-fold increased risk of ACS (5)
- Occurrence of acute coronary events 15 years earlier (5)
- A 2-fold increased short- (6,7) and long-term mortality (6,8)
- An increased incidence of post-infarction recurrent ischemic events, heart failure and cardiogenic shock (3,9)
- A similar benefit from guideline-recommended management strategies (see below)
- Less utilization of guideline recommended care (10–13), including an invasive strategy (14) which may contribute to adverse outcomes (15).

Risk Stratification of People With Diabetes and ACS

It is recognized that there is a wide range of risk for an adverse outcome in people with diabetes after an ACS. A recent study developed a prediction model that indicated age, renal dysfunction, the presence of anemia, heart failure or left ventricular (LV) dysfunction, in-hospital revascularization, obesity, prior ACS and insulin treatment were factors significantly associated with mortality during the 5 years after acute MI (AMI) (16).

Identification of Diabetes in People with ACS

Although the absolute number of people with MI has fallen in the United States, the prevalence of diabetes in this population has steadily increased from 18% in 1997 to 30% in 2006 (16). More than two-thirds of people with MI have either diabetes or prediabetes (impaired glucose tolerance [IGT] or impaired fasting glucose [IFG]) (17). Abnormal glucose regulation is almost twice as prevalent in people with MI compared to a matched control population and is a marker for adverse outcomes (18). The frequency of previously unrecognized diabetes in the ACS population is reported to be between 4% and 22% depending on the test used for the diagnosis of diabetes (3,19). If fasting plasma glucose (FPG) criteria is used alone in the ACS population, diabetes is underdiagnosed in 39% compared to when the diagnosis is made from an oral glucose tolerance test (OGTT) (20). An A1C >6.5% is currently a diagnostic criterion for diabetes as it captures long-term glucose exposure, does not require fasting or timed samples and is currently used to guide management decisions (see Screening for Diabetes in Adults chapter, p. S16). One study has validated the use of A1C in an acute care population and found that using the 2-hour 75 g OGTT as a gold standard for the diagnosis of diabetes, and an A1C threshold of 6.0%, A1C had a sensitivity of 77% and a specificity of 87% (21). It is accepted that some people with diabetes will be missed by screening with fasting plasma glucose (FPG) and A1C compared to the universal use of an OGTT. However, it is likely that the people most in

Conflict of interest statements can be found on page S193.

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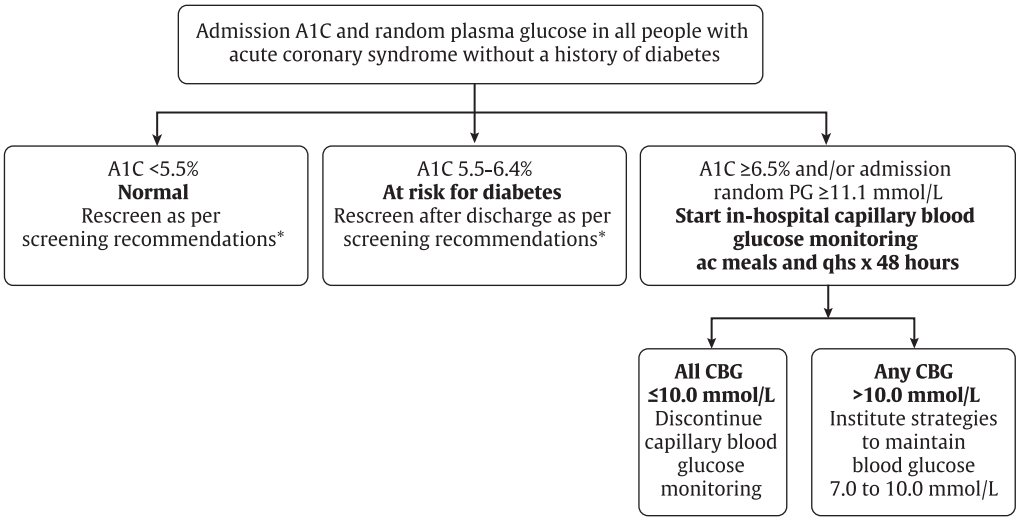

ACS, acute coronary syndrome; *BG*, blood glucose; *CBG*; capillary blood glucose; *CBGM*, capillary blood glucose monitoring; *PG*; plasma glucose.
*See Figure 1. Screening for Diabetes in Adults chapter, p.S16.

Figure 1. Screening for type 2 diabetes in people with ACS.

need of glycemic control will be detected with these simple tests that can be widely applied. In-hospital capillary blood glucose monitoring should be started in individuals without a history of diabetes with an admission A1C ≥6.5% or random plasma glucose (PG) >10.0 mmol/L. Individuals with an A1C between 5.5% to 6.4% should have repeat screening after discharge as per diabetes screening guidelines (see Screening for Diabetes in Adults chapter, p. S16 and Figure 1).

Management of ACS in People With Diabetes

Guidelines for the management of people with ACS have been developed by the American College of Cardiology/American Heart Association (22–24) and the European Society of Cardiology (25,26). In most situations, there are no clinical trials that specifically address management of people with diabetes and ACS; however, subgroup analyses in people with diabetes and ACS show either a similar or enhanced benefit from treatment compared to the overall group for: a) reperfusion with fibrinolysis (27) or primary angioplasty (28) for ST-segment elevation ACS; and b) an early invasive strategy (29) with the use of dual anti-platelet therapy with acetylsalicylic acid (ASA) and clopidogrel (30), glycoprotein IIb/IIIa inhibitors and the newer P2Y12 platelet inhibitors (prasugrel and ticagrelor) in people with non-ST segment elevation ACS at high risk of recurrent ischemic events (31).

A significant care gap exists for people with diabetes not receiving guideline-recommended treatment compared to people without diabetes (10–12,15,16). It is possible that the underutilization of recommended treatment is one factor contributing to the adverse outcome of the person with diabetes and ACS.

Anti-Platelet Therapy and ACS in People With Diabetes

Platelet aggregation plays a central role in the development of the occlusive thrombus responsible for acute coronary occlusion in people with ACS. People with diabetes have a pro-thrombotic state due to dysfunctional and hyperactive platelets, endothelial dysfunction, elevated coagulation factors and decreased fibrinolysis (32). Increased platelet activity is due to multiple metabolic and cellular factors associated with diabetes that include endothelial dysfunction, the impact of hyperglycemia and deficient insulin action (32).

Diabetes is associated with an increased incidence of recurrent atherothrombotic events (33), including stent thrombosis (34). Anti-platelet therapy has been shown to reduce atherothrombotic events in people with ACS, both during the acute phase and in the longer term. The beneficial effect of ASA has been shown in multiple clinical trials in patients with non–ST-segment elevation acute coronary syndrome (NSTE ACS) and ST-segment elevation MI (STEMI). The Antithrombotic Trialist's Collaboration meta-analysis (35) of anti-platelet therapy (mainly ASA) included 212,000 high-risk participants (with acute or previous vascular disease) and showed the incidence of vascular events to be reduced in both the overall population (16.8% to 12.8%; p<0.00001) and in the participants with diabetes (22.3% to 18.5%; p<0.002). Low-dose ASA (75 to 150 mg) was as effective as higher doses (>150 mg) with a lower incidence of bleeding complications. The Clopidogrel optimal loading dose Usage to Reduce Recurrent EveNTs-Organization to Assess Strategies in Ischemic Syndromes (CURRENT/OASIS 7) trial (36) also was unable to show any benefit from higher dose compared to low-dose (75 to 100 mg) ASA in people with and without diabetes. The use of low-dose ASA is recommended to minimize GI bleeding in people with and without diabetes (see Cardiovascular Protection in People with Diabetes chapter, p. S162).

Dual anti-platelet therapy with ASA and clopidogrel, administered from the time of presentation, has been the recommended standard of care for people with NSTE ACS. People with diabetes in the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial (30) had a similar benefit with clopidogrel vs. placebo (14.2% vs. 17.7%, RR 0.84, 95% CI 0.70–1.02) as the overall population (9.3% vs. 11.4%, RR 0.80, 95% CI 0.72–0.90). Despite dual-antiplatelet therapy with ASA and clopidogrel, recurrent atherothrombotic events continue to occur, especially in the person with diabetes. Clopidogrel is a relatively weak inhibitor of platelet aggregation with a wide variation of inhibition of in-vitro platelet aggregation. There is a higher incidence of events in people with residual platelet activity and people with diabetes have higher residual platelet activity despite ASA and clopidogrel treatment. Two more potent antiplatelet agents, prasugrel and ticagrelor, that are more effective and predictable inhibitors of platelet aggregation, have been shown to improve outcomes, especially in people with diabetes.