

## NEWLY DIAGNOSED DIABETES/HYPERGLYCEMIA IN HOSPITALS: WHAT SHOULD WE DO?

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### ABSTRACT

**Objective:** To examine the clinical problem of newly diagnosed diabetes/hyperglycemia in hospitals, and to develop a management strategy.

**Methods:** A review of the literature on outcomes and management of such patients.

**Results:** There are very few published papers on this subject, the majority being in patients with cardiovascular disease. However, there is recognition that the problem is common. No randomized clinic trials have been carried out on therapeutic strategies in such patients. The limited data available suggest that patients with newly diagnosed diabetes and hyperglycemia tend to have a poor prognosis.

**Conclusion:** Newly diagnosed diabetes/hyperglycemia in hospital is a common problem and is associated with a poor prognosis. Therefore, it seems appropriate that such patients be managed the same way as patients with established diabetes. Following discharge, appropriate diagnostic testing is needed to establish the presence or absence of diabetes so that long-term treatment plans can be initiated. (*Endocr Pract.* 2006;12[Suppl 3]:108-111)

### Abbreviation:

MI = myocardial infarction

### PREVALENCE AND IMPORTANCE

The importance of diabetes control has been widely recognized in terms of proving long-term complications. In the last 4 to 5 years, managing diabetes with tight glucose control also has led to improvements in outcomes for patients with critical illness in intensive care units as well as perioperatively, particularly during coronary artery bypass surgery. However, the impact of newly diagnosed diabetes in these situations, as well as that for patients admitted to the hospital with other medical problems, has not been well studied. Nevertheless, it appears that newly diagnosed hyperglycemia may be an indicator of prognosis. Therefore, studies are urgently needed to determine optimal management strategies in the effort improve outcomes in such patients.

The problem is relatively common, and with the increase in obesity and diabetes the general population, it is likely that a growing proportion of hospitalized patients will have hyperglycemia. In one study (1), hyperglycemia was present in 38% of patients admitted to the hospital, 26% of whom had a known history of diabetes and 12% had no history of diabetes before the admission. Patients with newly discovered hyperglycemia have been shown to have a significantly higher in-hospital mortality rate (16%) compared with patients who have a history of diabetes (3%) and subjects with normoglycemia (1.7%). In addition, new hyperglycemic patients have a longer hospital stay, a higher admission rate to an intensive care unit, and were less likely to be discharged to home, frequently requiring transfer to a transitional care unit or nursing home facility. Thus, it is essential to recognize that patients with newly diagnosed hyperglycemia have a significantly higher mortality rate and lower functional outcome than patients with a known history of diabetes or normoglycemia (1).

The effect of glycemic status on mortality has been best studied in patients with coronary artery disease. Muhlestein et al (2) demonstrated that, in patients undergoing coronary angioplasty, even mild elevations in blood glucose affect prognosis. Almost 70% of patients with their first myocardial infarction (MI) have either impaired glucose tolerance or undiagnosed diabetes (3). Conaway et al (4) showed that more than 50% of patients admitted with

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acute coronary syndromes have an abnormality of glucose metabolism. It is also recognized that blood glucose itself may rise transiently because of stress, but hemoglobin A1c (HbA1c) is a long-term indicator of glycemic status, and it predicts mortality in patients with MI not known to have diabetes (5).

Despite advances in interventional cardiology, patients with newly diagnosed hyperglycemia continue to have adverse outcomes (6,7). Acute hyperglycemia, but not diabetes, was a predictor for in-hospital mortality after MI. Reflow did not occur more frequently during angioplasty in patients with acute hyperglycemia (6).

The poor prognosis of patients newly diagnosed with hyperglycemia seems to persist even after discharge from the hospital. A recent study demonstrated that patients with hyperglycemia on admission for MI, independent of a history of diabetes, represent a high-risk population for 180-day mortality. The worst outcome occurs in nondiabetic hyperglycemic patients (8).

Patients with newly diagnosed hyperglycemia and moderate elevations in glucose are likely to have this diagnosis ignored during admission. This may be especially true for vulnerable populations, such as the elderly. Elevated glucose is common, rarely treated, and associated with increased mortality risk in elderly patients with acute MI, particularly those without recognized diabetes (9). Kosiborod et al (9) evaluated a national sample of elderly patients hospitalized with acute MI from 1994 to 1996. A substantial proportion of hyperglycemic patients (26% of those with glucose >240 mg/dL) did not have recognized diabetes. Fewer hyperglycemic patients without known diabetes received insulin during hospitalization than did diabetics with similar glucose levels. Higher glucose levels were associated with greater risk of 30-day mortality among patients without known diabetes compared with diabetics (9). After multivariable adjustment, higher glucose levels continued to be associated with a graded increase in 30-day mortality among patients without known diabetes (referent, glucose  $\leq$ 110 mg/dL; range, from glucose >110 to 140 mg/dL: hazard ratio [HR], 1.17; to glucose >240 mg/dL: HR, 1.87). In contrast, among diabetic patients, greater mortality risk was observed only in those with glucose >240 mg/dL (9).

#### **MANAGEMENT OF NEWLY DIAGNOSED HYPERGLYCEMIA**

Unfortunately, newly diagnosed diabetes or hyperglycemia is frequently ignored in the hospital (9), and patients often are discharged with other diagnoses but without a plan for management of this condition. This is regrettable because such a diagnosis may represent an opportunity to institute a plan for long-term diabetes management that, if initiated early, could lead to prevention of complications.

The management of hyperglycemia in such patients might be difficult because many patients have underlying insulin resistance, particularly the critically ill (10). Recent data suggest that a pancreatic beta cell defect also may be present, with implications for treatment (11). Among 168 consecutively treated patients with acute MI, beta cell responsiveness to glucose deteriorated with decreasing glucose tolerance (11,12). Glucose abnormalities were very common in patients with MI but without previously known type 2 diabetes. To a significant extent, this appears to relate to impaired beta cell function and implies that dysglycemia immediately after MI is not a stress epiphenomenon but rather reflects stable disturbances of glucose regulation preceding the MI. Early beta cell dysfunction might have important pathophysiologic implications and may serve as a future target for treatment strategies.

Several studies have demonstrated beneficial effects of insulin on outcomes, particularly when the blood glucose is maintained near normal. In addition, intensive insulin therapy is associated with suppression of markers of inflammation. Chaudhuri et al (12) demonstrated that the effects of insulin in patients with MI who did not have diabetes insulin infusion led to lower elevations of inflammation markers and less myocardial damage.

The principals of managing patients with newly diagnosed hyperglycemia or diabetes remain the same as those for patients with well-known and established diabetes. Every effort should be made to mimic the normal daily physiologic insulin profile using a basal-bolus approach and attempting to mimic first-phase insulin secretion. For patients who are eating, multiple daily injections using insulin analogs is probably the most appropriate therapy. The long-acting basal insulin could be rapidly up-titrated to meet a fasting glucose target. It is important to recognize that insulin requirements frequently are high in type 2 diabetes and may be higher still in patients who are critically ill. It is important to give sufficient glucose to prevent hypoglycemia. However, if the given glucose is not kept within the normal range, insulin may be ineffective. In the presence of normoglycemia, insulin has been shown to have very important effects on inflammation and oxidative stress (13).

When introducing an aggressive management strategy, it is also important to recognize the risks of hypoglycemia. This condition has been associated with cardiovascular mortality (14). In the setting of acute coronary syndromes among patients with diabetes, both hyperglycemia on arrival and hypoglycemia during hospitalization are independently associated with the worse-adjusted, all-cause, 2-year mortality risk (14). These observations suggest that the avoidance of both hyper- and hypoglycemia may be of similar importance, and that glucose modulation remains an important objective to address in future randomized trials. Responses to hyperglycemia, such as contra-regula-

tory hormone secretion, may have cardiac effects. Lack of energy substrates may cause further tissue ischemia. Finally, a study in patients with insulin treatment and known coronary artery disease showed more ischemic events occurring during hypoglycemia or when there was a rapid decrease in blood glucose (15).

Table 1 outlines the plan for the inpatient stay, which essentially should focus on confirming the diagnosis and controlling hypoglycemia, preferably using an insulin infu-

sion. Comorbidities (including lipid abnormalities, diabetes complications, and the presence of microalbuminuria) should be evaluated because they are important prognostic indicators. Complications such as retinopathy are important to recognize if anticoagulants have been used.

The patient should be referred for diabetes education and nutrition therapy, either in the hospital or within a short time of discharge. The discharge plan (Table 2) should emphasize the diagnosis of diabetes, if it has been established,

<b>Table 1</b> <b>Plan for Inpatient Stay: Patients With Newly Diagnosed Hyperglycemia</b>
<ul style="list-style-type: none"> <li>• Check HbA1c to confirm long-standing diabetes</li> <li>• Rapidly control hyperglycemia – insulin infusion</li> <li>• Check for associated comorbidities                             <ul style="list-style-type: none"> <li>– Lipids may not be representative of long-term status</li> <li>– Microalbuminuria is a good prognostic indicator</li> <li>– Look for retinopathy, particularly if using anticoagulants</li> <li>– Look for nephropathy before using contrast media</li> </ul> </li> <li>• Refer patients for diabetes education and medical nutrition therapy, either in the hospital or within a short time post discharge; this is a “teachable moment”</li> </ul> <p><i>Plan for Inpatient Stay – Insulin</i></p> <ul style="list-style-type: none"> <li>• Insulin therapy most suitable for rapid glycemetic control – high doses often needed</li> <li>• Insulin still required when NPO</li> <li>• Basal-bolus therapy most appropriate when eating</li> <li>• Insulin must balance food; schedule dosing only with meals and not at fixed times</li> <li>• To avoid hypoglycemia, use short-acting analogs with or even after the meal</li> <li>• Insulin sensitizers may be needed for insulin-resistant or steroid-treated patients</li> </ul>

<b>Table 2</b> <b>Plan for Discharge: Patients With Hyperglycemia</b>
<ul style="list-style-type: none"> <li>• Emphasize the diagnosis of diabetes again</li> <li>• Discharge plans should have clear recommendations for the short- and long-term management of glycemia</li> <li>• Follow-up diabetes education</li> <li>• Eye examination for patients newly diagnosed with type 2 diabetes</li> <li>• Consider ACEI and statins, per guidelines</li> </ul>

and provide clear recommendation for both short- and long-term management of glycemia. Because patients will not assimilate much information while in the hospital, particularly if they have been newly diagnosed, follow-up diabetes education should be planned. It is also important to schedule an eye examination for newly diagnosed patients with type 2 diabetes and to consider angiotensin-converting enzyme inhibitors (ACEI) and statin drugs according to established guidelines.

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