American College of Endocrinology and American Diabetes Association Consensus Statement on Inpatient Diabetes and Glycemic Control

A call to action

THE ACE/ADA TASK FORCE ON INPATIENT DIABETES*

Diabetes has reached epidemic proportions in the U.S., affecting in excess of 20 million individuals (more than one of every three persons). In addition, another 26% have impaired fasting glucose (1). Similarly, a disproportionate number of hospitalized patients have diabetes. Furthermore, for every two patients in the hospital with known diabetes, there may be an additional patient with newly observed hyperglycemia (2,3). Compelling evidence continues to accumulate to suggest that poorly controlled blood glucose levels are associated with increased morbidity and mortality, as well as with higher health care costs. In 2002, 4.9 million hospital discharges in the U.S. were associated with diabetes (4). The cost of inpatient diabetes care for 2002 was estimated at $40 billion—the single largest component of direct medical costs for the disease (5).

Until recently, glycemic control in hospitalized patients has not been a major therapeutic focus, partly because of a lack of published targets and guidelines for management of such patients and partly because evidence demonstrating improved overall outcomes as the result of improved glycemic control was only just emerging. In 2004, the American College of Endocrinology (ACE) and the American Association of Clinical Endocrinologists (AACE) published the first recommendations for the management of inpatient diabetes and metabolic control (6). The American Diabetes Association (ADA) supported an extensive technical review evaluating the relationships between glycemic control and its effect on hospital outcomes (7). This review became the basis for the 2005 ADA Clinical Practice Recommendations (8).

Notwithstanding national and local efforts, widespread implementation of improved glycemic control for inpatients has remained an elusive goal for many medical centers. Multiple institutional and attitudinal obstacles still exist to improving health care, and these barriers have created a substantial and growing gap between what we know and what we actually do. For this reason, ACE and ADA joined forces and convened a consensus conference (Inpatient Diabetes and Glycemic Control: A Call to Action Conference), with the goal of identifying strategies to overcome barriers and facilitate improvements in inpatient diabetes care.

SPECIFIC CONSIDERATIONS — In an effort to focus our considerations, a series of questions were addressed.

Question 1: Does improving glycemic control improve clinical outcomes for inpatients with hyperglycemia?

For many years, epidemiologic and uncontrolled observational data have associated acute and chronic hyperglycemia with adverse inpatient outcomes. More recently, interventional studies have linked reversal of hyperglycemia to better clinical outcomes in medical and surgical patients, especially in the setting of acute myocardial infarction (MI), cardiac surgi-

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cal procedures, infection, and critical illness (9–18).

Data derived from surgical and medical intensive care units. In a study of critically ill and mixed medical and surgical intensive care unit (ICU) patients, the use of intensive insulin therapy to achieve arterial whole blood glucose levels of 80–110 mg/dl reduced mortality by 34%, sepsis by 46%, renal failure necessitating dialysis by 41%, need for blood transfusion by 50%, and critical illness-related polyneuropathy by 44% (11).

New data regarding "tight" glycemic control in the medical ICU has recently been published (19). Similar to the original investigation from the surgical ICU, patients who required a prolonged ICU stay (>3 days) benefited significantly from the attainment of euglycemia in comparison with the conventionally treated control group, with reduced mortality (52.5 vs. 43.0%; relative risk reduction 18.1%; $P = 0.009$). In the entire study cohort (an intent-to-treat analysis), improvements were noted in several ICU-related morbidities (such as renal dysfunction and prolonged mechanical ventilation), but mortality was not significantly reduced (40.0 vs. 37.3%; relative risk reduction 6.8%; $P = 0.33$). Among the 433 patients who were in the ICU fewer than 3 days, mortality was 18.8 vs. 26.8% in the conventionally and intensively treated groups, respectively. After adjustments for baseline characteristics, including APACHE (Acute Physiological Assessment and Chronic Health Evaluation) II score, this difference was not statistically significant ($P = 0.41$). Although generally consistent with the surgical ICU data, the increased early mortality, albeit not statistically significant, will necessitate further investigation through either post hoc analysis of these data or further studies in this area (19). Of note, arterial blood glucose levels were used to establish the targets and large differences may exist among arterial, venous, and capillary blood glucose values.

- A study of 1,600 patients admitted to a medical-surgical ICU evaluated outcomes associated with improved glycemic control (13). The insulin infusion group had improved blood glucose levels in comparison with a retrospective control group: 130.7 vs. 152.3 mg/dl, respectively ($P < 0.001$). Those patients with reduced blood glucose levels had associated significant reductions in mortality and median duration of ICU stay.
- A recent meta-analysis of 35 clinical trials evaluating the effect of insulin therapy on mortality in hospitalized patients with critical illness found that insulin therapy decreased short-term mortality by 15% in a variety of clinical settings (14).

Data derived from patients with acute MI

- In patients with acute MI, elevated glucose levels are a predictor of mortality in patients with and without diabetes (16,20). In addition, elevated glucose levels have been associated with larger infarct size in patients without a prior history of diabetes who were being treated with perfusion therapy for ST-segment elevation MI (21).
- A meta-analysis of 15 studies of patients who were hospitalized for acute MI reported that blood glucose levels in excess of 110 mg/dl were associated with proportionally greater mortality and increasing rates of congestive heart failure (22).
- In the first DIGAMI (Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction) study (15), patients with acute MI received intravenous insulin therapy for 24 h, followed by multiple daily injections of insulin for ≥3 months, and had a 29% reduction in mortality at 1 year and a 28% reduction at 3.4 years in comparison with the control group.
- The DIGAMI 2 study (23) was designed to compare three treatment strategies in patients with acute MI: group 1 received acute insulin-glucose infusion followed by insulin-based long-term glucose control; group 2 received insulin-glucose infusion followed by standard glucose control; and group 3 received routine metabolic management in accordance with local practice. Unfortunately, this study did not reach recruitment goals and showed no treatment differences. Moreover, the primary treatment target of a fasting blood glucose level of 90–126 mg/dl for those in group 1 was never achieved. Mean fasting blood glucose levels (149 mg/dl) and HbA_{1c} (A1C) (6.8%) were similar among the three study groups. Thus, if glycemia is predictive of outcomes, no differences would have been expected, and no differences were observed.
- In the CREATE-ECLA (Clinical Trial of Metabolic Modulation in Acute Myocardial Infarction Treatment Evaluation–Estudios Cardiologicos Latinoamerica) trial (24), >20,000 patients with ST-segment elevation MI were treated with a 24-h glucose-insulin-potassium infusion or placebo, irrespective of baseline glucose. Glucose-insulin-potassium infusion did not improve mortality; however, the relative hyperglycemia that resulted in active therapy may have obscured any treatment benefit.

As shown in these last two studies, insulin infusion in the absence of blood glucose lowering clearly has no effect on outcomes.

Data derived from cardiac surgical patient populations. Hyperglycemia is an independent predictor of infection in patients with diabetes undergoing a cardiac surgical procedure (25). Furthermore, hyperglycemia during the first 48 postoperative hours was associated with a two-fold higher rate of surgical-site infections among patients undergoing a cardiothoracic operation in comparison with surgical patients who had normal blood glucose levels (17).

Good glycemic control in patients undergoing a cardiac surgical procedure results in an improved outcome. Furnary et al. (10) investigated the effect of continuous insulin infusions in comparison with the prior use of intermittent subcutaneous insulin injections in patients with diabetes undergoing a cardiac operation. In patients given insulin intravenously during the perioperative period, the risk of deep sternal wound infection was reduced by 57%. A subsequent analysis (12) reported that intensive glucose control was associated with a 66% reduction in mortality; the lowest mortality was observed in patients with a mean postoperative blood glucose level <150 mg/dl.

Hyperglycemia in hospitalized medical and surgical patients. Observational studies suggest an association between hyperglycemia and poor clinical outcomes in general medical and surgical patients.

- Pomposelli et al. (26) found that a single blood glucose level >220 mg/dl on the 1st postoperative day is a sensitive predictor of nosocomial infection.
- A retrospective review of medical records of 1,886 hospitalized patients conducted by Umpierrez et al. (3) revealed an 18-fold increase in mortality in patients with hyperglycemia without a prior history of diabetes and a 2.5-fold increase in mortality in patients with

known diabetes in comparison with that in control subjects.
- A meta-analysis of 26 studies by Capes et al. (27) reported that an admission blood glucose level >110 mg/dl was associated with increased mortality in patients who were hospitalized for acute stroke.

Thus, the expansion of the database that has occurred since our first consensus conference on inpatient diabetes and metabolic control (6) shows findings consistent with, and strengthens our views regarding, the importance of inpatient glycemic control.

Question 2: Is cost a barrier to improved inpatient care?

Cost is often perceived as a barrier to excellent inpatient glycemic control because achieving strict control safely and effectively necessitates efforts that seem to be relatively expensive and labor intensive and that require coordination of the services of many hospital divisions. A more appropriate perspective, however, would be gained by examining the cost-effectiveness of this care. Utilization of hospital services should be viewed as an investment, rather than an expense, inasmuch as improved glycemic control ultimately results in cost savings, as noted in the subsequent material. In 2002 in the U.S., direct inpatient costs for patients with diabetes were $40.3 billion (5). Hyperglycemia itself has been shown to contribute to increasing hospital length of stay (LOS) and overall cost. Investigators have shown that for each 50-mg/dl increase in blood glucose level in patients with diabetes undergoing a coronary artery bypass grafting procedure, there was an additional 0.76-day LOS (an incremental hospital cost of $2,824) (28). Hyperglycemia is an independent predictor of hospital LOS in trauma patients (29).

Controlling hyperglycemia in patients with either previously diagnosed diabetes or newly discovered hyperglycemia in the hospital has been shown to be cost-effective in many different settings.

- The use of a diabetes team consultation resulted in a 56% reduction in hospital LOS, for a cost reduction of $2,353 per patient (30).
- In cardiac surgical patients, implementation of intensive glycemic control with use of intravenous insulin protocols resulted in a substantial decrease in sternal wound infections and subsequent decrease in both cost and hospital LOS when compared with historical data (10,31).
- Use of an intensive insulin management protocol in the surgical ICU resulted in improved medical outcomes, with a reduction of ICU stay resulting in an estimated yearly cost savings of $40,000 per ICU bed (11). Although the cost of intensive insulin therapy was nearly double the cost of the conventional treatment, the excess cost of intensive insulin management was more than offset by a 25% reduction in the total hospitalization cost (32).
- In North Carolina, Newton (33) showed that in the medical ICU, intensive glycemic control resulted in a reduction of mean blood glucose level from 169 to 123 mg/dl, with a resultant decrease in catheter-related sepsis by 33.5% and achievement of substantial cost savings. He also reported that lowering the mean blood glucose level from 177 to 151 mg/dl was associated with a reduction in hospital LOS from 6.01 to 5.75 days (0.26 days); during the same time interval, there was no reduction in hospital LOS in patients without hyperglycemia. This reduced LOS allows the hospital to serve more patients per bed and generates further income from new patient diagnosis-related groups. The "throughput value," calculated as incremental inpatient volume multiplied by revenue margin, was $2.2 million/year for this hospital.
- At an academic medical center, financial cost-modeling analysis of the benefit of intensive diabetes management was performed both for critical care units and for medical and surgical wards with use of a dedicated diabetes team approach. Substantial savings were possible because of better documentation, reduced hospital LOS, and generation of new revenues (T. Balczak, unpublished data).
- The use of an intensified glycemic protocol by a diabetes management team in Oklahoma resulted in correct coding and treatment of patients with previously unrecognized hyperglycemia. Hospital LOS was reduced for both primary and secondary diagnoses, and readmission rates declined (34).

Therefore, these examples show that optimizing glycemic management is not only medically effective, saving lives and reducing morbidity, but also cost-effective to health care systems.

Question 3: Has inpatient management of diabetes become a quality and safety concern?

Quality. Inpatient management of hyperglycemia and avoidance of hypoglycemia have become important measures of the quality of health care afforded to hospitalized patients. Translation of the evidence regarding glycemic management that has been derived from multiple clinical trials into performance metrics will be useful in inpatient settings throughout the U.S. and elsewhere. Performance measures will be important tools for widespread assessment and benchmarking of quality of diabetes care and will be a key motivator for improvement of quality. Development of performance measures will necessitate agreed-upon definitions of quality based on translation of available evidence into valid, feasible, reproducible, and actionable performance metrics for both internal quality improvement and external accountability.

- A compendium of tested tools and strategies is needed to assist facilities as they implement programs for glycemic control at their sites. The cosponsors of the current consensus conference have agreed to develop a Web site, accessible through multiple cosponsoring organizations, that contains a guidebook to implementation with a collection of protocols, standing orders, and other educational tools to assist in the initiation of tested programs for improved glycemic control.
- The National Diabetes Quality Alliance is encouraged to develop performance measures for inpatient management of hyperglycemia in patients with and without diabetes. The development of measures that can be used internally by medical centers and hospitals for quality improvement and the development of measures robust enough for use for external accountability are recommended. This consensus conference also encourages the Alliance to submit the performance measures to the National Quality Forum for the approval process, which then would establish these measures as standards for the nation.
- When available, we encourage purchasers, payers, and accreditors to adopt nationally standardized measures for use in their publicly reported measure sets (e.g., ORYX), their disease management accreditation programs (e.g., the new Joint Commission on Ac-

creditation of Healthcare Organizations –ADA Advanced Disease Management Certification), and their pay-for-performance programs (such as the Centers for Medicare and Medicaid Services demonstrations and publicly reported measure sets as part of their Hospital Compare program).

Safety. Both under- and overtreatment of hyperglycemia are safety issues in the hospitalized patient. Unrecognized and untreated hyperglycemia is an "error of omission" because hyperglycemia creates an unsafe setting for the treatment of illness and disease. Undertreatment may occur as a result of failure to treat pronounced hyperglycemia or inappropriate withholding of insulin doses. The fear of hypoglycemia is a barrier to adequate care, and yet the risk of hypoglycemia may actually be reduced by a policy of intensive glucose management. Nevertheless, overtreatment of hyperglycemia leading to hypoglycemia remains a major safety issue. The Joint Commission on Accreditation of Healthcare Organizations considers insulin to be one of the five highest risk medicines in the inpatient setting. For enhanced safety, medication errors must be documented, analyzed, and tracked. A systems approach to analyzing hospital processes is essential, and a "culture of safety" must exist that is embraced by all involved parties.

Some of the common sources of errors that threaten the safety of hospitalized patients include the following:

- Lack of coordination between feeding and administration of medications, leading to mistiming of insulin action
- Insufficient frequency of blood glucose monitoring
- Orders not clearly or uniformly written
- Failure to recognize the need for changes in insulin requirements because of advanced age, renal failure, liver disease, change in clinical status, use of corticosteroids, or interruption or changes in feeding

A systems approach to reducing errors in insulin therapy in the inpatient setting has recently been described (35). Strategies to minimize medical errors that can lead to safety issues include the use of the following:

- Electronic medical records
- Computerized physician order entry
- Checklists
- Written protocols
- Improved communication between caregivers, especially in transitions of care, including discharge from the hospital

Avoiding the common sources of errors and implementing systems to detect them can improve patient safety and enhance the quality of care.

Question 4: What are the systematic barriers and challenges to improved management of hyperglycemia?

Many of the changes needed to improve the management of inpatients with hyperglycemia involve alterations in culture, long-standing practice patterns, processes of care, and work-flow habits. Competing priorities and limited resources can present a major barrier to the institutional support that is essential to a successful improvement effort. Other organizational barriers are as follows.

- Incremental nursing time and effort needed can be a burden on nursing systems. The current national nursing shortage magnified by inadequate support systems may make this situation more difficult. Nurses are essential for successful implementation of protocols, order sets, more intensive glucose monitoring, and educational programs targeting enhanced glycemic control.
- Skepticism about the benefits of good inpatient glycemic control remains a barrier to rapid adoption of attempts to implement change, despite the preponderance of evidence suggesting that it is beneficial. This situation may be exacerbated by a general resistance to change.
- Fear of hypoglycemia is a major barrier to efforts to improve glycemic control.
- Inadequate knowledge and understanding of diabetes, hyperglycemia, and appropriate management of blood glucose levels also represent a barrier. Educational programs for providers and inpatients involve time-consuming efforts.
- Lack of integrated information systems that allow tracking and trending of glycemic control and hypoglycemia metrics can thwart the implementation of glycemic management programs. Improvement teams are faced with the task of devising regular reports to summarize and trace the trends of variables that describe glycemic control or hypoglycemia rates in the absence of standardized methods to do so.

Diabetes and hyperglycemia are prevalent on all services in the hospital; thus, broad educational efforts and changes in processes are necessary. Because patients frequently move across a spectrum of care providers and geographical locations during a single inpatient stay, multiple "handoffs," communication challenges, and opportunities for error exist. The complexity of the task of achieving safe handoffs and consistency in the approach across this spectrum of care is a substantial challenge. A lack of ownership for management of hyperglycemia contributes to the challenges of glycemic control because most patients are admitted to the hospital for reasons other than hyperglycemia (36).

Question 5: What strategies are effective for achieving improved management of diabetes in hospitalized patients?

Successful implementation of a program to improve glycemic control in the inpatient setting should include the following components (37):

1) An appropriate level of administrative support
2) Formation of a multidisciplinary steering committee to promote the development of initiatives
3) Assessment of current processes, quality of care, and barriers to necessary changes in practice
4) Development and implementation of interventions, including standardized order sets, protocols, policies, and algorithms with associated educational programs
5) Metrics for evaluation

Administrative support. To improve glucose control in the hospital setting, the management of patients with diabetes or hyperglycemia must become an institutional priority. Achieving this goal involves enlisting administrative support for the long-term investment of both time and resources from multiple individuals and departments. The most salient means of demonstrating this commitment is through the establishment of a multidisciplinary steering committee that is empowered to develop and guide processes for improving glycemic control in hospitalized patients. Supportive data are avail-

able for the financial and clinical benefits of such programs.

Multidisciplinary steering committee. A multidisciplinary steering committee should be charged with assessing and monitoring the quality of glycemic management within the institution. Members of this team should include all key stakeholders. Ideally, participants should include medical staff; nursing and case management, pharmacy, nutrition services, dietary, laboratory, quality-improvement, and information systems personnel; and administration.

Assessment of current processes, quality of care, and barriers to necessary changes in practice. This assessment step involves an investigation of current practices and policies and how they affect glycemic control. Hospitals should systematically track glucose data to assess the quality of care delivered. Personnel from information systems and other departments can help identify data sources to obtain information for accurate assessment of glycemic control before and after implementation of specific protocols. Identification of organizational structure, culture, and resources will help guide the plan for protocol development and approach to implementation.

Development and implementation of interventions. Protocols or algorithms and order sets should be developed to guide the management of hyper- and hypoglycemia throughout the hospital. An educational effort for both staff and patients, with ongoing assessment of efficacy and safety, is essential. To achieve any established target reliably, a standardized protocol is necessary.

The best intravenous insulin protocols take into account several factors, including the current and previous blood glucose levels (and, therefore, the rate of change) and the current insulin infusion rate. The intensive approach to glucose control with insulin infusion necessitates frequent (usually hourly) blood glucose determinations. Several published insulin protocols are available (38–41). The exact protocol is probably less important than its presence in an institution, adaptation to the specific hospital, adequate support from key local opinion leaders and implementation staff, and ultimate validation.

With tight glycemic control, an increase in frequency of hypoglycemia is expected. In this setting, it is typically rapidly diagnosed, mild, transient, and not clearly associated with any adverse outcomes. The benefit of intravenous insulin infusion in critically ill patients, in whom intensive monitoring is available, far outweighs any potential risk. If a protocol does not seem to be effective in a specific patient, then urgent input is needed from a clinician with expertise in diabetes management. Standardization across the institution should be considered for practical and logistical reasons. Finally, the important transition to subcutaneous administration of insulin must be an integral part of any insulin infusion protocol.

During the initial implementation of an insulin infusion protocol, it is important to educate all staff about the importance of tight glycemic control in critically ill patients and to engage them in the process. Specifically, those personnel implementing the protocol should be asked to help troubleshoot when specific concerns arise. Preprinted algorithms or computerized systems and adequate technical support should be available. During the early phase, appropriate expert support should be readily available. Protocols should be periodically reviewed to ensure that they continue to meet the needs of the hospital and its patients.

Many patients who are not critically ill may benefit from intensive management similar to that in the ICU setting. Some institutions have successfully implemented insulin infusion protocols safely on general wards with modifications, including intensive staff education and adequate staff support. Without these important factors, however, intensive insulin infusion becomes difficult and potentially dangerous in this setting. An alternative approach to intravenous insulin therapy is physiologic subcutaneous insulin therapy, which may be the most practical method for achieving glycemic control outside of the ICU setting. Targets should be individualized for patients with severe comorbidities, particularly if life expectancy is reduced and in those at risk for hypoglycemia (elderly, malnourished, or cognitively impaired patients or those with liver and renal failure).

Several approaches to antihyperglycemic therapy have been proposed for general hospital wards. It is generally agreed that in many circumstances, orally administered agents are not appropriate for in-hospital use. In stable patients who are eating, orally administered agents may be used, but only after careful consideration of the anticipated stability of the patient's nutritional status and the potential for any adverse effects.

The traditional regular insulin "sliding scale" is not recommended, particularly when used as the sole type of insulin therapy. This "retrospective" form of insulin replacement is inherently illogical and has been associated with increased glycemic excursions. Moreover, in certain settings, such as in patients with type 1 diabetes, it is potentially very dangerous. There may be a role for its selective use in patients with newly recognized hyperglycemia with an unknown insulin requirement or with initiation of other therapies associated with elevations in blood glucose levels (for example, enteral nutrition, corticosteroids, or octreotide); however, this application might be more accurately described as the use of "correction insulin."

Instead, standardized order sets promoting the use of scheduled insulin therapy should be used. Basal replacement insulin therapy (that is, NPH, glargine, or detemir) is advised, in conjunction with nutritional or prandial short- or rapid-acting insulin (that is, regular, aspart, lispro, or glulisine). Additional "correction insulin" added to the short- or rapid-acting insulin (same type) is also widely used. Examples of this method are available in the literature (42). Provisions for special patient circumstances, including "nothing by mouth" status, parenteral and enteral nutrition, and corticosteroid therapy, should be addressed by algorithms and educational efforts. Protocols should suggest starting dose and adjustment strategies. Aggressive and frequent dosing changes are necessary to achieve glycemic control during hospitalizations.

One intervention that may be considered to facilitate control of hyperglycemia is a specific glycemic management clinical team. The timely consultation of such a team has been demonstrated to improve quality of care, reduce hospital LOS, and lower costs. Such teams offer subspecialty assistance for those patients who do not achieve adequate glycemic control with use of protocols alone. Whether the team focuses on every patient with hyperglycemia or simply those not quickly achieving blood glucose targets is best decided on the basis of local culture and needs.

Hypoglycemia remains a major impediment to achieving glucose control. Appropriate standardized treatment protocols that address mild, moderate, and severe hypoglycemia should be an automatic part of all order sets for patients treated with insulin or insulin secreta-

gogues. With these protocols in place, and with the recognition that most hypoglycemia is mild, transient, and easily treated, appropriate glycemic control is achievable.

Medical nutrition therapy is another integral part of inpatient hyperglycemia management. A nutritional plan outlined by a registered dietitian and a meal plan focusing on consistent carbohydrate consumption are suggested. In light of the caloric requirements of patients who are ill, the adequacy of nutritional intake always must be ensured. Restriction of calories is not the appropriate strategy for control of blood glucose levels; instead, adequate insulin therapy should be administered.

Diabetes self-management education is also an important component in the management of patients with hyperglycemia. Self-management knowledge and skills should be assessed and appropriate interventions provided by individuals trained in diabetes care. Survival skills education should be delivered in the inpatient setting, with follow-up education and self-management support scheduled as needed after dismissal from the hospital. An essential link at the time of dismissal is communication with the outpatient provider. Too often, little or no communication occurs, a situation that can result in lack of follow-up or inappropriate care such as the discontinuation of insulin therapy in patients in whom it should be continued.

Measurement of A1C at the time of admission can be useful for the assessment of preadmission diabetes control and to assist in guiding the transition to outpatient management (43).

A smooth inpatient-to-outpatient transition is critical. Appropriate discharge planning with identification of subsequent glycemic management plans and follow-up should be explicit. Goal-directed glycemic management in the hospital will serve as a model for the patient's self-directed care after discharge. Importantly, even when intensive regimens are used in the hospital, the ultimate discharge regimen must take into account the motivations and capacities of the patient. Nevertheless, the anticipated compliance as an outpatient should not dissuade aggressive inpatient glycemic control, especially during prolonged hospitalizations.

Metrics for evaluation. A system to track hospital glucose data on an ongoing basis should be implemented to assess the quality of diabetes care delivered. The availability of such a mechanism will drive the continuous improvement of processes and protocols for glycemic management.

Question 6: What management strategies can be implemented in patients identified with hyperglycemia in the hospital?

Patients with hyperglycemia can be classified into one of three categories: previously diagnosed diabetes, unrecognized diabetes, or hyperglycemia related to hospitalization (a problem that is relatively common).

Unfortunately, both newly noted hyperglycemia and established diabetes are frequently ignored in the hospital, with patients often discharged without a plan for evaluation and management of these conditions. This clearly is detrimental to the patient because such a diagnosis may represent an opportunity to institute a plan for long-term glycemic control; if initiated early, such an intervention may lead to prevention of complications. More than 50% of patients admitted with acute coronary syndromes have abnormal glucose metabolism (44,45). Recently, the Euro Heart Survey (46) of >2,000 patients showed that the majority of those with coronary artery disease had abnormal glucose metabolism. Furthermore, almost 70% of patients with their first MI have either impaired glucose tolerance or undiagnosed diabetes (45). Inpatient hyperglycemia may be an indicator of prognosis, and the routine use of an oral glucose tolerance test to identify at-risk coronary artery disease patients may provide the opportunity for preventive care. A1C is a long-term indicator of glycemic status and also predicts mortality in patients with MI who are not known to have diabetes (47).

The principles of glucose management in patients with newly detected hyperglycemia remain the same as those for patients with established diabetes. The discharge recommendations for those with newly recognized glucose abnormalities must emphasize a plan to evaluate the cause of the hyperglycemia. Many of these patients will indeed have diabetes or at least pre-diabetes, which necessitates ongoing observation. Pre-diabetes also presents an opportunity for evidence-based prevention of diabetes, and such interventions may also prevent cardiovascular events. A clear care plan should be developed for short- and long-term testing, survival skills education, follow-up, and management.

Question 7: What areas need further research?

Questions and issues to address

1) What are the central mechanisms underlying the development and exacerbation of hyperglycemia in the hospitalized patient?

- Counterregulatory hormones
- Increased hepatic glucose production
- Decreased glucose utilization (peripheral insulin resistance)
- Diminished tissue perfusion
- Peripheral insulin resistance
- Increased circulating free fatty acids
- Inflammation (cytokines)

2) By what mechanisms does hyperglycemia produce harm?

- Glycemic variability and increased free radical production
- Metabolic processes
- Glucosamine
- Polyol pathways
- Hexose monophosphate shunt
- Glycation products and their reactive products
- Oxidative stress
- Inflammation (cytokines)
- Nuclear factor-κβ
- Superoxide generation

Understanding these mechanisms may help develop additional targets for therapy.

3) What research is needed to improve practical aspects of achievement of inpatient glycemic control?

- Refinement of insulin protocols
- Glucose sampling sites, methodology, and frequency
- Closed-loop systems
- Continuous glucose monitoring
- The role of feeding: enteral and parenteral
- Improvement of protocols for transitioning to subcutaneously administered insulin after transfer from the ICU
- Role of orally administered agents: alone and in combination with insulin
- Strategies to minimize hypoglycemia
- Transition from in-hospital "basal-bolus" insulin therapy to a discharge regimen

4) What further randomized controlled trials are needed to document the benefits of glycemic control?

- Optimal glycemic targets for patients in medical and surgical wards: desirable end points would include hypoglycemia rates, in-hospital complications, readmission rates, and long-term glycemic control
- Additional medical ICU studies
- Use of insulin sensitizers in the inpatient setting
- Use of intensive insulin therapy in special populations of patients with hyperglycemia (e.g., cancer patients, age extremes, diverse ethnic backgrounds, socioeconomic status)

In the performance of these studies, the differences among arterial, venous, and capillary blood glucose values should be clearly identified, and a standard for future research should be defined.

5) What are strategies for discharge planning that support maintenance of glycemic control?

- Insulin versus orally administered agents for long-term management
- Lifestyle modification (nutrition and exercise)
- Self-care behaviors
- Continuity of care

APPENDIX

Task Force

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The American College of Endocrinology and the American Diabetes Association.

Cosponsors

The American Association of Critical-Care Nurses, the American Association of Diabetes Educators, the American Heart Association, the American Society of Anesthesiologists, the Joint Commission on Accreditation of Healthcare Organizations, the Society of Critical Care Medicine, the Society of Hospital Medicine, and the Veterans Health Administration.

Participating Organization

The American College of Cardiology.

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