

## Hospital Dysglycemia and the Importance of Nutrition Therapy

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### INTRODUCTION

As the global diabetes epidemic continues to grow, so does the number of hospitalized patients with diabetes and hyperglycemia. Dysglycemia, in the form of hyperglycemia, hypoglycemia and glycemic variability, is common and associated with poor clinical outcomes in hospitalized patients. However, observational and randomized controlled studies demonstrate that better glycemic control improves outcomes, including lower rates of hospital complications. The development of effective strategies, including nutrition strategies, is imperative for effective glycemic management in the hospitalized patient.

### HOSPITAL DYSGLYCEMIA: A MARKER FOR QUALITY OF CARE

Dysglycemia, which can be an indicator of poor quality of care, increases the risk for adverse outcomes in surgical patients and common clinical conditions including stroke and critical illness. For example, acute hyperglycemia predicts increased risk of in-hospital mortality after ischemic stroke and increases the risk of poor functional recovery.<sup>1</sup> In critically ill patients, increased glycemic variability is an independent risk factor for mortality, increasing the risk by 2- to 5-fold.<sup>2,3</sup> In surgical patients, perioperative hyperglycemia increases the incidence of systemic blood infections, surgical site infections, acute renal failure, and postoperative mortality.<sup>4-7</sup>

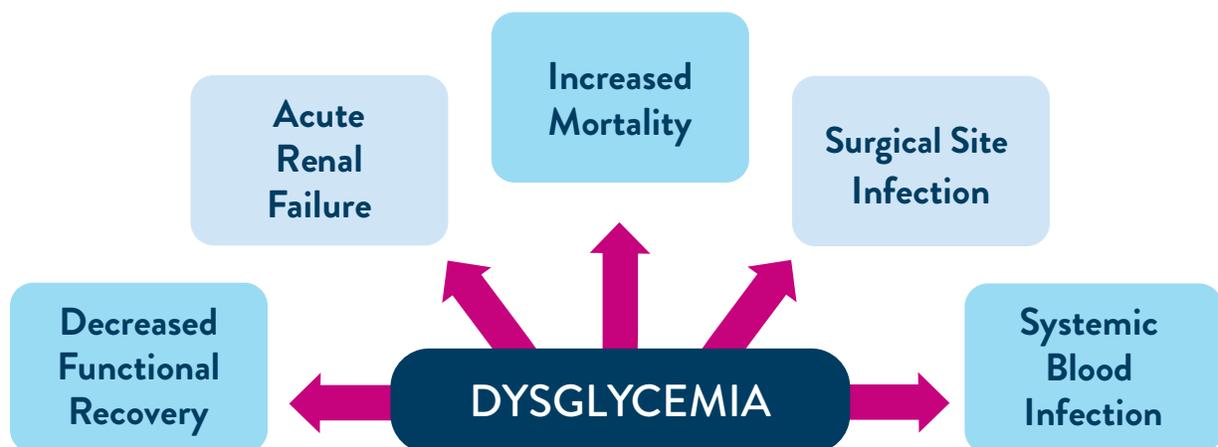


Figure 1: Dysglycemia can lead to poor patient outcomes

Dysglycemia in the form of **hyperglycemia** is common in hospitalized patients, with reports indicating that up to 38% of hospitalized patients develop persistent hyperglycemia, and up to 80% of intensive care unit (ICU) patients experience stress-induced hyperglycemia.<sup>8-10</sup>

Dysglycemia in the form of **hypoglycemia** is also common, with 12%-18% of hospitalized patients experiencing at least one episode (<60 mg/dL).<sup>8</sup> A retrospective study by Lipska et al<sup>11</sup> found that the rates of admissions for hypoglycemia increased from 94 to 105 admissions per 100,000 from 1999 to 2011. Hypoglycemia rates were also doubled for patients ≥ 85 years of age. Turchin and colleagues<sup>12</sup> conducted a retrospective analysis of 4,368 general hospital ward admissions. Hypoglycemia was common among the 2,582 patients with diabetes, and was associated with increased length of stay and higher mortality during and after admission.

A growing body of evidence suggests that dysglycemia in the form of glycemic variability is also common, and can adversely impact patient outcomes. Glycemic variability, defined as acute glucose fluctuations around a mean value, can independently impact hospital length of stay and mortality.<sup>2,3,13-15</sup>

## STRATEGIES FOR IMPROVED GLYCEMIC CONTROL IN THE HOSPITAL AND THE ROLE OF NUTRITION THERAPY

Managing hyperglycemia in the hospital is critical to improving outcomes, and hyperglycemia is an indicator for quality of care. Actions to help improve glycemic management in hospitalized patients include:

- establish protocols for glycemic control;
- use an interdisciplinary team approach to diabetes management;
- create systems to identify and manage dysglycemia;
- educate staff on current diabetes management; and
- optimize nutrition therapy.

Nutrition therapy is a key component in the comprehensive management of diabetes and hyperglycemia in the hospital setting. The American Diabetes Association specifies that two key goals of nutrition therapy for hospitalized patients are to: 1. optimize glycemic control, and 2. provide adequate nutrients to meet metabolic demands.<sup>16</sup> Hospitalized patients with diabetes who cannot maintain their nutritional requirements through oral intake alone often require tube feedings with an enteral formula.

Since hyperglycemia is often a side effect of enteral nutrition support, initiation of tube feeding can be challenging when managing glucose levels. The administration of enteral or parenteral nutrition is an independent risk factor for the onset of or the exacerbation of hyperglycemia independent of a prior history of diabetes.<sup>17-19</sup> Furthermore, newly diagnosed hyperglycemia in hospitalized patients is reportedly an independent prognostic factor of mortality in enterally fed patients.<sup>20</sup> Therefore, appropriate selection and administration of an enteral formula is an important part of medical management.

Nutritional requirements of patients with diabetes receiving tube feeding can be met with the use of standard or glycemia-targeted nutritional (GTN) enteral formulas, often referred to as diabetes-specific formulas. In addition to providing nutrients to meet nutrition goals, GTN formulas are designed to attenuate blood glucose responses better than standard formulas.

Many standard enteral formulas have high levels of low molecular carbohydrates, which are rapidly digested and can thus increase postprandial glucose responses in people with diabetes.<sup>21-24</sup> Unlike standard formulas, GTN formulas have a modified macronutrient profile and low glycemic carbohydrates that help minimize postprandial glycemic responses, thereby supporting blood glucose management. Studies have shown that GTN formulas can improve glycemic outcomes better than standard formulas, including postprandial glycemic response, mean glucose, and glycemic variability.<sup>21,24-28</sup> The use of GTN formula can also reduce insulin requirements,<sup>24,29,30</sup> and can have economic benefits, including reduced length of stay and lower hospital costs.<sup>31,32</sup>

### GLYCEMIA-TARGETED NUTRITIONAL (GTN) FORMULAS AND GLYCEMIC OUTCOMES

GTN formulas are better than standard formulas to help improve glycemic outcomes in people with hyperglycemia and/or diabetes. Numerous studies have demonstrated that the use of GTN versus standard formulas or common breakfast foods produces a better glycemic response.<sup>21,23,24</sup>

Elia and colleagues<sup>21</sup> conducted a meta-analysis of 23 studies to evaluate the effects of standard versus diabetes-specific enteral formulas. The diabetes-specific formulas were associated with better glucose responses than standard formulas, producing significantly lower postprandial increases in blood glucose, peak blood glucose concentrations, and glucose area under the curve (AUC) in patients with diabetes.

In 2014, Ojo and colleagues<sup>33</sup> found similar outcomes in a systematic review of randomized controlled trials comparing diabetes-specific formulas with standard formulas. Diabetes-specific formulas were more effective in controlling glucose profiles including postprandial glucose, HbA1c, and insulin response.

Studies also support the use of GTN formulas to help manage glucose levels in patients with hyperglycemia and/or diabetes. The use of GTN versus standard formula resulted in positive clinical outcomes including:<sup>24,25,27-30,34</sup>

- lower mean glucose;
- reduced glycemic variability;
- reduced hypoglycemia; and
- reduced insulin requirements.

For example, Mesejo et al<sup>30</sup> conducted a prospective, randomized, open label, multicenter trial evaluating diabetes-specific versus standard formula in 157 hyperglycemic ICU subjects on mechanical ventilation. Patients on a GTN versus standard formula had significantly reduced insulin requirements ( $P<0.05$ ), improved glycemic control ( $P<0.01$ ), reduced hypoglycemia (50-80 mg/dL,  $P<0.05$ ), and lower risk of acquired infections ( $P<0.05$ ). These data support the clinical value of GTN formulas for minimizing glycemic excursions in hospitalized patients.

Based on the evidence, an ESPEN (European Society for Clinical Nutrition and Metabolism) expert group recently published recommendations related to carbohydrates and insulin resistance in clinical nutrition:

*“Based on this available evidence, the ESPEN expert group endorses the utilization of diabetes-specific formulas (DSFs) for nutritional support of people with obesity and diabetes.”<sup>35</sup>*

## GLYCEMIA-TARGETED NUTRITIONAL (GTN) FORMULAS AND HEALTH ECONOMICS AND OUTCOMES RESEARCH

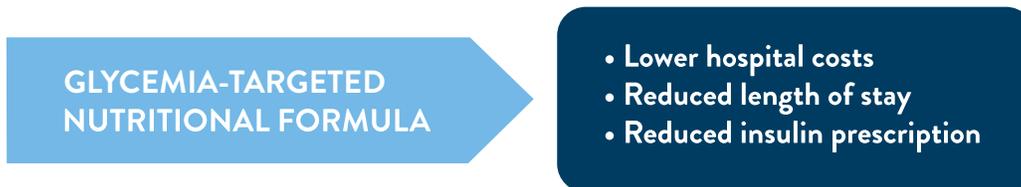


Figure 2: Glycemia-targeted nutrition is associated with lower healthcare costs

The use of GTN formulas is also associated with lower healthcare costs.<sup>32,36,37</sup> Diabetes imposes a large economic burden on a nation's healthcare system, with healthcare expenditures for diabetes care accounting for 11.6% of the world's total healthcare expenditure in 2015.<sup>38</sup> For patients with diabetes, hospital inpatient care has been reported as the largest component of medical expenditures (43% of the total medical cost).<sup>39</sup> Health economic studies have demonstrated the benefits of GTN versus standard formulas, based on outcomes such as length of stay and healthcare cost. These health economics and outcomes research studies promote a holistic understanding of the economic impact of GTN formulas as a component of overall diabetes management.

Hamdy and colleagues<sup>32</sup> evaluated hospital length of stay and hospital cost of GTN versus standard formulas for tube-fed patients with diabetes during acute-care hospitalizations. This 10-year (2000-2009) retrospective analysis of 85,481 hospital inpatients comprised 20% of all US hospitalizations of patients with diabetes. Propensity score matching and multivariable regression analysis revealed that the administration of GTN versus standard formulas to tube-fed patients with diabetes was associated with a nearly 1-day shorter adjusted length of hospital stay ( $P < 0.0001$ ) and lower hospital costs per patient (\$2,586 USD). The authors concluded that feeding GTN formula to patients with diabetes was associated with significantly improved healthcare efficiency.

Han et al<sup>31</sup> found similar results in a retrospective study of 2087 ICU records covering a 5-year period (2009-2013) from the hospitalization database of the National Taiwan University Hospital. The use of GTN versus standard enteral formula in critically ill patients with diabetes was associated with decreased mortality, fewer prescriptions for insulin, and a savings of \$2,500 USD/patient in total ICU cost. Both studies support the economic benefits of GTN versus standard formula in hospitalized patients with diabetes.<sup>31,32</sup>

### CONCLUSION:

The continued growth of the global diabetes epidemic is accompanied by increases in the number of hospitalized patients with diabetes and hyperglycemia. Effective nutrition strategies, including the appropriate selection and administration of enteral tube feeding, are needed to support glycemic control and improve health economic outcomes in this population. The growing body of literature helps guide clinical decision making regarding the selection of an enteral formula to support glycemic management. Additional research in the hospital setting is needed to further guide clinical decisions and formula selection for the hospitalized patient.

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