EMR-Based Tool for Identifying Type 2 Diabetic Patients at High Risk for Hypoglycemia

Karter AJ, Warton M, Lipska KJ, et al. Development and validation of a tool to identify patients with type 2 diabetes at high risk of hypoglycemia-related emergency department of hospital. JAMA Intern Med 2017 Aug 21.

Study Overview

Objective. To develop and validate a risk stratification tool to categorize 12-month risk of hypoglycemia-related emergency department (ED) or hospital use among patients with type 2 diabetes (T2D).

Design. Prospective cohort study.

Setting and participants. Patients with T2D from Kaiser Permanente Northern California were identified using electronic medical records (EMR). Patients had to be 21 years of age or older as of the baseline date of 1 January 2014, with continuous health plan membership for 24 months prebaseline and pharmacy benefits for 12 months prebaseline. Of the 233,330 adults identified, 24,719 were excluded for unknown diabetes type, and 3614 were excluded for type 1 diabetes. The remaining 206,435 eligible patients with T2D were randomly split into an 80% derivation sample (n = 165,148) for tool development and 20% internal validation sample (n = 41,287). Using similar eligibility criteria, 2 external validation samples were derived from the Veterans Administration Diabetes Epidemiology Cohort (VA) (n = 1,335,966 adults) as well as from Group Health Cooperative (GH) (n = 14,972).

Main outcome measure. The primary outcome was the occurrence of any hypoglycemia-related ED visit or hospital use during the 12 months postbaseline. A primary diagnosis of hypoglycemia was ascertained using the following *International Classification of Diseases, Ninth Revision* (ICD-9) codes: 251.0, 251.1, 251.2, 962.3, or 250.8, without concurrent 259.3, 272.7, 681.xx, 686.9x, 707.a-707.9, 709.3, 730.0-730.2, or 731.8 codes [1]. Secondary discharge diagnoses for hypoglycemia were not used because they are often attributable to events that occurred during the ED or hospital encounter.

Main results. Beginning with 156 (122 categorical and 34 continuous) candidate clinical, demographic, and behavioral predictor variables for model development, the final classification tree was based on 6 patient-specific variables: total number of prior episodes of hypoglycemia-related ED or hospital utilization (0, 1–2, ≥ 3 times), number of ED encounters for any reason in the prior 12 months (< 2, ≥ 2 times), insulin use (yes/no), sulfonylurea use (yes/no), presence of severe or end-stage kidney disease (dialysis or chronic kidney disease stage 4 or 5 determined by estimated glomerular filtration rate of ≤ 29 mL/min/1.73 m^2 (yes/no), and age

younger than 77 years (yes/no). This classification tree resulted in 10 mutually exclusive leaf nodes, each yielding an estimated annual risk of hypoglycemia-related utilization, which were categorized as high (> 5%), intermediate (1%–5%), or low (< 1%).

The above classification model was then transcribed into a checklist-style hypoglycemia risk stratification tool by mapping the combination of risk factors to high, intermediate, or low risk of having any hypoglycemia-related utilization in the following 12 months.

Regarding patient characteristics, there were no significant differences in the distribution of the 6 predictors between the Kaiser derivation vs. validation samples, but there were significant differences across external validation samples. For example, the VA sample was predominantly men, with a higher proportion of patients older than 77 years, and had the highest proportion of patients with severe or end-stage kidney disease. Regarding model validation, the tool performed well in both internal validation (C statistic = 0.83) and external validation samples (VA C statistic = 0.81; GH C statistic = 0.79).

Conclusion. This hypoglycemia risk stratification tool categorizes the 12-month risk of hypoglycemia-related utilization in patients with T2D using 6 easily obtained inputs. This tool can facilitate efficient targeting of population management interventions to reduce hypoglycemia risk and improve patient safety.

Commentary

It is estimated that 25 million people in the United States have diabetes [2]. Hypoglycemia is a frequent adverse event in patients with T2D, being more common than acute hyperglycemic emergencies such as hyperosmolar hyperglycemic state [3]. Iatrogenic hypoglycemia due to glucose-lowering medication can result in hypoglycemic crisis that requires administration of carbohydrates, glucagon, or other resuscitative actions in the ED or in hospital [4,5]. The estimated total annual direct medical costs of hypoglycemia-related utilization were estimated at approximately $1.8 billion in the United States in 2009.

The risk of hypoglycemia varies widely in patients with T2D and there are no validated methods to target interventions to the at-risk population. In this article, Karter and colleagues developed and validated a pragmatic hypoglycemia risk stratification tool that uses 6 factors to categorize the 12-month risk of hypoglycemia-related ED or hospital utilization.

Identifying patients at high-risk for hypoglycemia-related utilization provides an opportunity to mobilize resources to target this minority of patients with T2D, including deintensifying or simplifying medication regimens, prescribing glucagon kits or continuous glucose monitors, making referrals to clinical pharmacists or nurse care managers, and regularly asking about hypoglycemia events occurring outside the medical setting. This is important, as more than 95% of severe hypoglycemia events may go clinically unrecognized because they did not result in ED or hospital use [6]. In addition, as the 6 inputs were identified by EMR, intervention can include automated clinical alert flags in the EMR and automated messaging to patients with elevated risk.

Several limitations exist. The study excluded secondary discharge diagnoses for hypoglycemia as these may occur due to sepsis, acute renal failure, trauma, or other causes. In addition, the external validation populations had different distributions of disease severity and case mix. The authors attribute some of the inconsistent findings to sparse data in the GH validation sample (n = 14,972). Finally, this tool was developed to stratify the population into 3 levels of risk, and it should not be used to estimate the probability of hypoglycemic-related utilization for an individual patient.

Applications for Clinical Practice

The EMR-based hypoglycemia risk stratification tool categorizes the 12-month risk of hypoglycemia-related utilization in patients with T2D using 6 easily obtained inputs. This tool can facilitate efficient targeting of population management interventions, including integration into existing EMR as clinical decision aid, to reduce hypoglycemia risk and improve patient safety.

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Oral Corticosteroids for Acute Lower Respiratory Infection: Are We Ready to Drop This Practice?

Hay AD, Little P, Harnden A, et al. Effect of oral prednisolone on symptom duration and severity in nonasthmatic adults with acute lower respiratory tract infection: a randomized clinical trial. JAMA 2017;318:721–30.

Study Overview

Objective. To assess the effects of oral corticosteroids for acute lower respiratory tract infection in adults without asthma or COPD.

Design. Multi-center, placebo-controlled, randomized clinical trial.

Setting and participants. This study was conducted at 4 UK centers (the Universities of Bristol, Southampton, Nottingham, and Oxford) between July 2013 and October 2014. Patients with acute cough (≤ 28 days) and at least 1 of the following lower respiratory tract symptoms (phlegm, chest pain, wheezing, or shortness of breath) were recruited by family physicians and nurses. Patients with chronic pulmonary disease, who had received asthma medication in the past 5 years, required hospital admission, or required same-day antibiotics were excluded. Patients were randomized by variable block size into prednisolone or placebo groups in a 1:1 ratio, stratified by center.

Intervention. Participants were asked to take 2 tablets of either 20-mg oral prednisolone or placebo tablets once daily for 5 days. The medications, which looked and tasted identical, were packaged into numbered packs by an independent pharmacist and were delivered to the family practices to be distributed to the enrolled patients. Participants were invited to report daily, using web or paper version, the severity of symptoms using a scale 0 to 6, along with twice-daily peak flow, for 28 days or until symptom resolution. Participants received shopping vouchers. Medical notes were reviewed at 3 months for new diagnosis of asthma, chronic obstructive pulmonary disease, whooping cough, and lung cancer.

Main outcome measures. The primary outcomes were the duration of moderately bad or worse cough (defined as the number of days from randomization to the last day with a score of at least 3 points prior to at least 2 consecutive days with a score of less than 3, up to a maximum of 28 days); and the mean severity score (range 0–6) of the 6 main symptoms (cough, phlegm, shortness of breath, sleep disturbance, feeling generally unwell, and activity disturbance) on days 2 to 4.

Main results. 401 patients were randomized; 25 patients were lost to follow-up, leaving 173 in prednisolone group and 161 in placebo group for analysis. The prednisolone group was slightly more likely to be male, older, and to have received an influenza vaccine. 96% were white. Symptom diaries were returned by 94% of patients. For primary outcome 1, duration of moderately bad or worse cough, the median time to recovery from moderately bad or worse cough was 5 days (interquartile range, 3–8 days) in both groups. There was no difference after sensitivity analysis (multiple imputation of missing data, per-protocol analysis, and adjusting for day of recruitment). Primary outcome 2, the mean symptom severity score, after adjustment for center and baseline measure, was lower (hazard ratio, –0.20) in the prednisolone group compared with the placebo group; however, after secondary additional adjustment for age, sex, influenza vaccine, and smoking, the difference was not statistically significant. Secondary