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ORIGINAL ARTICLE

The SQuID protocol (subcutaneous insulin in diabetic ketoacidosis): Impacts on ED operational metrics

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Abstract

Background: Studies using fast-acting subcutaneous (SQ) insulin analogs in diabetic ketoacidosis (DKA) have demonstrated efficacy, safety, and cost-effectiveness, allowing treatment of mild-to-moderate (MTM)-severity DKA patients in non–intensive care unit (ICU) settings. However, emergency department (ED)-based studies are few, with limited exploration of impacts on operational metrics.

Methods: We implemented the SQuID (Subcutaneous Insulin in Diabetic Ketoacidosis) protocol for adults with MTM-severity DKA in an urban academic ED, collecting data from August 1, 2021, to February 28, 2022. We examined fidelity (frequency of required q2h glucose checks), safety (proportion of patients administered rescue dextrose for hypoglycemia), and ED length of stay (EDLOS) for the SQuID cohort compared to patients (non-ICU) treated with a traditional insulin infusion. We also examined ICU admission rate among MTM-severity DKA patients after introduction of SQuID to two historical control periods (pre-intervention and pre-COVID). We used Mann–Whitney U to test for differences in EDLOS distributions, bootstrapped ($n = 1000$) confidence intervals (CIs) for EDLOS median differences, and the two-sample z-test for differences in ICU admissions.

Results: We identified 177 MTM-severity DKA patients in the study period (78 SQuID, 99 traditional cohort) and 163 preintervention and 161 pre-COVID historical control patients. Fidelity to the SQuID pathway was good, with glucose checks exceeding the q2-h requirement. We found no difference in the proportion of rescue dextrose administration compared to the traditional pathway. We observed significant reductions in median EDLOS for the SQuID cohort compared to the traditional cohort during the study period (−3.0, 95% CI −8.5 to −1.4), the preintervention period (−1.4, 95% CI −3.1 to −0.1), and the pre-COVID control period (−3.6, 95% CI −7.5 to −1.8).

Conclusions: In this single-center study at an academic ED, treatment of patients with MTM-severity DKA with a SQ insulin protocol was effective, demonstrated equivalent safety, and reduced ED length of stay.

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KEYWORDS
diabetic ketoacidosis, emergency, subcutaneous insulin

INTRODUCTION

Diabetic ketoacidosis (DKA) is a common, dangerous condition accounting for a major source of mortality in patients with type 1 and increasingly type 2 diabetes.[1,2] In 2018 DKA accounted for 223,000 ED visits or 8.9 ED visits per 1000 adults with diabetes.[3] DKA results in over 500,000 annual hospital days with estimated annual hospital costs of $5.1 billion.[4] While mortality and hospital length of stay (HLOS) related to DKA appear to be decreasing, incidence, hospitalizations, and associated costs are significantly increasing.[4–8]

Though the treatment of DKA is well established, coordinating safe and effective management is complex. This involves careful attention to fluid resuscitation, electrolyte replacement, administration of an intravenous (IV) infusion of insulin and hourly blood glucose checks for monitoring response to therapy.[9–11] Because of the intensity of monitoring and management steps involved, and potential safety concerns with insulin infusions, treatment of mild-to-moderate (MTM) DKA typically requires admission to an intensive care unit (ICU) or an intermediate care unit, with hospital policies in many facilities disallowing the use of IV insulin infusions outside these settings.[12,13] In many centers, ICUs are a limited resource, used for only the most severely ill of patients, with known variability in their use for DKA and increasing demand, particularly since the onset of the COVID pandemic.[12–17] Consequently, in many busy hospitals, patients with MTM-severity DKA are often managed in the emergency department (ED) until sufficiently improved (anion gap closed, IV insulin infusion discontinued) for admission to a medical floor. This results in lengthy stays in the ED, where hourly monitoring and adjustments compete for physician and nursing attention with other life-threatening illnesses, including stroke, trauma, and myocardial infarction, increasing the potential for adverse events (AEs) for all patients.

The past 20 years has witnessed the development of fast-acting insulin analogs that are highly effective in DKA, offering new treatment options for MTM-severity DKA that might obviate some of the issues associated with insulin infusions. A total of five small randomized controlled trials (20–50 patients, total patients 201; three ED-based, one pediatric ED-based), comparing subcutaneous (SQ) fast-acting insulin protocols to insulin infusions have been considered in three systematic reviews (albeit with low- or very-low-quality evidence ratings from Cochrane) showing equivalent time to resolution of DKA, safety in terms of hypoglycemic episodes and HLOS.[18–25] One adult and one pediatric study showed reductions in ICU utilization with a SQ protocol leading to cost reductions.[23,26] Another study demonstrated reduced costs treating DKA patients in a stepdown unit compared to an ICU.[27]

Taken together, these studies suggest that SQ treatment protocols for MTM-severity DKA are a promising safe alternative to traditional insulin infusions that could streamline care. In the context of limited ICU availability, ED and hospital crowding, and the requirement that patients on insulin infusions must go to the ICU or intermediate care unit, SQ insulin protocols may be able to decrease ED length of stay (EDLOS), helping decompress crowded EDs by (1) allowing patients who would otherwise wait in the ED until they could be weaned off an insulin infusion to go to a medical floor and (2) provide a non-ICU option for a MTM-severity DKA patient who might otherwise be waiting for an ICU in the ED. We are not aware of any studies focusing primarily on the impact of a SQ insulin protocol on EDLOS. Though the prevalence of the management of DKA in non-ICU settings is not reported, this practice does not appear to enjoy wide adoption. One editorial observed that

> … change in current practice will go much more smoothly if done using an approved hospital protocol. By managing some DKA patients in [non-ICU settings], we can anticipate equivalent patient outcomes while also increasing the availability of ICU care for other critically ill patients. As the new approach is gradually adopted in hospitals across the country, I hope that researchers will collect before–after data so that we can better understand the actual impact of this practice change on patients, providers, and the overall health care system.[25]

This is the direction we aimed for in the present study.

METHODS

Study design

This is a prospectively-derived quasi-experimental (pre–post) study evaluating the impact of the SQuID protocol on care for MTM DKA patients. We use retrospectively obtained electronic data in evaluating our outcome measures (fidelity, safety, and operational measures). This study was reviewed and approved by multiple hospital diabetes and pharmacy committees and was approved by our hospital institutional review board prior to initiation of the study with a waiver of consent. SQ insulin for DKA was considered an existing standard of care rather than an experimental protocol based on the published literature.

Setting

This study took place in an urban academic hospital with over 90,000 annual ED visits, serving a patient population reflecting

a continuum of acute to chronic and primary to critical care, and a spectrum of patient demographics, including many vulnerable populations. Our facility has no medical intermediate care unit and disallows the use of insulin infusions outside the ICU due to safety concerns.

Study population

ED patients meeting criteria for MTM-severity DKA (hyperglycemia, positive ketone test, presence of an anion gap) were eligible for the study. We stratified DKA severity as mild, moderate, or high severity, modified from a widely used scheme by Kitabchi et al.[11] (Figure 1A) where severity is driven by the highest discriminatory item. DKA patients were identified retrospectively based on laboratories including a blood glucose > 300 mg/dL, ketones ≥ 1.1 mmol/L, and presence of an anion gap acidosis or a discharge diagnosis of DKA and having received insulin. Patients with severe DKA (HCO_3 < 10 mmol/L or arterial pH < 7.0), less than 18 years of age were excluded from the analysis. Exclusion criteria for the SQuID protocol included pregnancy, concomitant serious infections, concerns for myocardial infarction, altered mental status, active comorbidities (end-stage renal disease, congestive heart failure, active use of immunosuppressants), need for a surgical procedure, or determination by the ED or inpatient team that a patient was too ill for the designated floor (an inpatient observation unit run by hospitalist physicians). The default pathway for patients with any of these exclusions is treatment with a traditional insulin infusion (Figure 1B).

Historical controls, selected primarily for comparisons of ICU admission rates, were identified using the same inclusion/exclusion criteria for the following two time periods: November 1, 2020, to May 31, 2021 (preintervention), and August 1, 2019, to February 28, 2020 (pre-COVID).

Study protocol

Our clinical protocol is outlined in Figure 1A and the study's clinical pathway is provided in Figure 2A. Our standard practice, predating this study, includes a question at triage of all patients as to whether they are diabetic. All diabetic patients have blood glucose testing performed, and if above 300 mg/dL, this prompts point-of-care ketone testing. If this is positive (above 1.1 mmol/L), additional laboratories are protocolled including a basic metabolic panel, whole blood potassium, and a venous blood gas. As part of implementing the SQuID protocol, the order for ketone testing also launched a best practice advisory (BPA) in our electronic medical record (EMR; Epic) to notify the clinician of potential candidates for the pathway.

The DKA BPA includes a reminder about SQuID, eligibility information, and a link to an order set with the SQuID protocol. The SQuID order set specifies every 2-h fingerstick blood glucose checks (rather than hourly blood glucose checks required when on an insulin infusion) and administration of SQ fast-acting insulin per the protocol (below) based on the blood glucose values. After ED evaluation is complete, a bed order is placed for admission to a cohorted inpatient floor for continued monitoring and therapy. Upon leaving the ED, SQuID patients are cared for on an inpatient observation unit staffed by the hospital medicine service with a dedicated nursing pool and a goal for discharge within 48 h. Patients would not be eligible for the SQuID pathway if a bed on the target floor was not available at the time this decision was being made. During the study period all patients being admitted required COVID testing and resulting.

(A) SQuID Protocol for Mild to Moderate DKA

- Check POC glucose every 2 hours and follow pathway below based on current glucose level
- BMP q4h → if K is LESS THAN 3.5, hold insulin until PRN K repletion
- Notify provider when the anion gap is 16 or less on repeat BMP to be transitioned from SQuID to maintenace insulin regimen

BG ≥ 250	1. Administer insulin lispro 0.2 units/kg subcutaneous 2. Continue 0.45% NS at 150 mL/hr
First BG < 250	1. Administer insulin lispro 0.1 units/kg subcutaneous 2. Decrease 0.45% NS to 50 mL/hr and continue until protocol is complete 3. Add D5W based on parameters below: • BG 200-250: START D5W at 100 mL/hr • BG 150-199: START D5W at 150 mL/hr • BG 100-149: START D5W at 200 mL/hr • BG <100: START D5W at MAX 250 mL/hr and NOTIFY PROVIDER
Subsequent BG after D5W initiated	1. Administer insulin lispro: ≥ 250 = 0.2 units/kg OR < 250 = 0.1 units/kg subcutaneous 2. After D5W is initiated, TITRATE D5W q2 hours with each blood glucose check as follows: • BG greater than 250: DECREASE D5W rate by 50 mL/hr • BG 200-250: KEEP D5W at same rate • BG 150-199: INCREASE D5W rate by 50 mL/hr • BG 100-149: INCREASE D5W rate by 100 mL/hr • BG <100: INCREASE to MAX 250 mL/hr and NOTIFY PROVIDER; repeat BG in 30-60 minutes from rate change
BG LESS THAN 70	1. Assess Patient • Alert/able to eat/drink: Give 15 grams of fast-acting carbohydrate (15 gm oral glucose, 4 oz. juice NOT ORANGE JUICE) • Unable to take PO - has IV access: D10W 250 mL over 15 min • Unable to take PO - no IV access: Give 1 mg Glucagon IM, obtain IV access, turn patient on side to prevent aspiration. Follow glucagon treatment with glucose treatment or IV dextrose 2. After treatment of hypoglycemia, NOTIFY PROVIDER, check blood glucose every 15 minutes, and repeat protocol until blood glucode is greater than 100

SEVERITY INDEX

Measure	DKA Severity		
	Mild	Moderate	Severe
Plasma Glucose Level	> 300	> 300	> 300
Arterial or Venous pH	7.25-7.30	7.0-7.24	< 7
Bicarbonate Level, mmol/L	15-18	10-14	< 10

(B) "Traditional" IV Infusion DKA Protocol

- Send whole blood K+. Do not give insulin until K is 3.5 or greater
- Initiate 2 L 0.9% NS bolus then start 0.45% NS at 150 mL/hr
- Insulin regular bolus - 0.1 units/kg ONCE intravenous (no max)
- Insulin regular - 0.1 units/kg/hr (max 10 units/hr)

INSULIN INFUSION	MAX DOSE: 10 UNITS IVP FOR BOLUS AND 10 UNITS/HR FOR INFUSION	
BG Decreased or Same as Last Value		
BG > 250	Continue infusion at current rate	
BG 151-250	If BG decreased 75 or more: 1. Decrease infusion rate by 50% 2. Add D5W at 100 mL/hr 3. Decrease 0.45% NS to 50 mL/hr	If BG decreased less than 75: 1. Continue infusion at current rate 2. Add D5W at 100 mL/hr 3. Decrease 0.45% NS to 50 mL/hr
BG 100-150	1. Decrease insulin drip by 50% 2. Notify provider 3. Add D5W at 100 mL/hr if not already started 4. Decrease 0.45% NS to 50 mL/hr if not already done	
BG 70-99	1. Hold infusion 2. Notify provider 3. Add D5W at 100 mL/hr if not already started 4. Decrease 0.45% NS to 50 mL/hr if not already done	
BG Increased Since Last Value		
BG "HI"	1. Send serum glucose to lab 2. Titrate up or maintain current infusion rate based on result, may exceed max dose	
BG > 250	Increase infusion rate by 50%	
BG 151-250	Continue infusion at current rate	
BG 100-150	1. Decrease infusion rate by 50% 2. Notify provider	
BG 70-99	Continue to hold infusion	
BG < 70	1. Hold infusion and notify provider 2. Give 250 mL D10W IVPB over 15 minutes 3. Check BG q15min 4. Once BG > 100 mg/dL, restart insulin drip with rate reduced by 50%	

When Anion Gap 16 or Less on Repeat BMP Obtain Transition Orders
- Administer Lantus 0.3 units/kg/day subcutaneous
- Insulin drip remains infusing 2 hours after Lantus administration then discontinue at 2hr mark
- Obtain discontinue order 2 hours after Lantus administration for D5W and 0.45% NS

FIGURE 1 (A) SQuID protocol for mild to moderate DKA. (B) "Traditional" IV infusion DKA protocol. DKA, diabetic ketoacidosis; EDLOS, emergency department length of stay; SQuID, subcutaneous insulin in diabetic ketoacidosis.

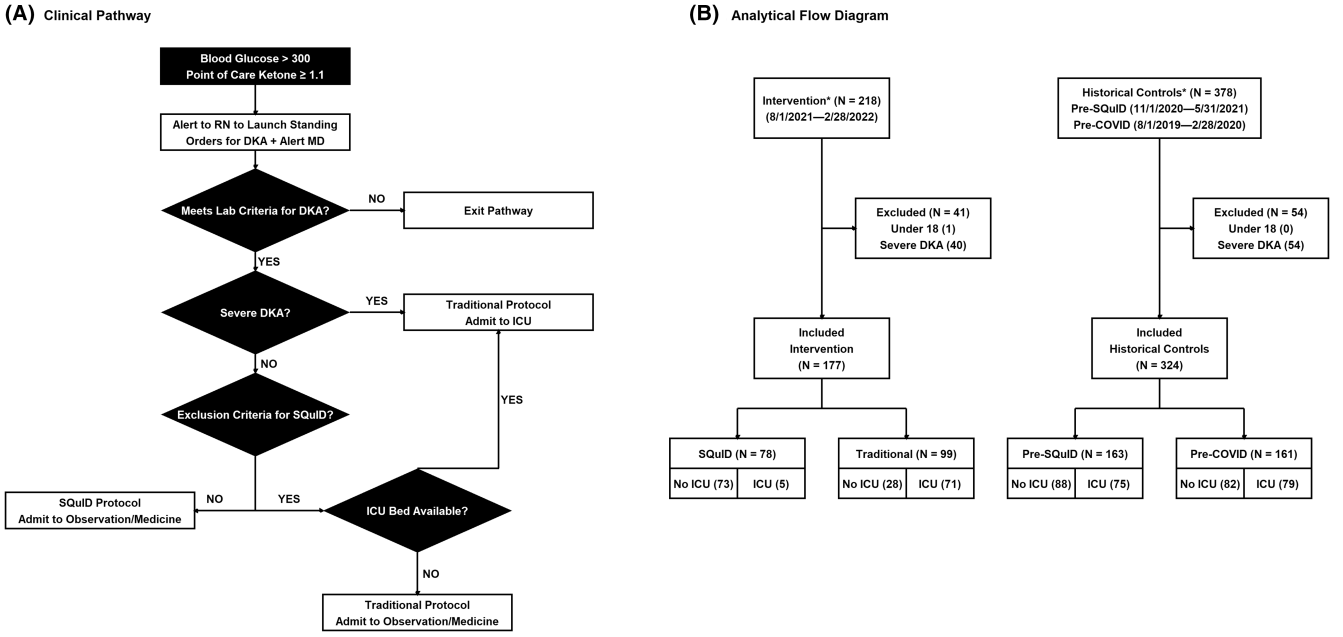

FIGURE 2 (A) Clinical pathway. (B) Analytical flow diagram. DKA, diabetic ketoacidosis; EDLOS, emergency department length of stay; ICU, intensive care unit; SQuID, subcutaneous insulin in diabetic ketoacidosis.

Education and training

Providers and nurses were educated on the SQuID protocol with the plan that this would be the default treatment pathway for appropriate patients. Education sessions included presentation at residency didactic sessions, ED and hospitalist faculty meetings, dissemination of a slide set with the protocol, presentations at ED RN morning and evening huddles, and dedicated educational sessions on the medical floor.

Data collection

The SQuID protocol was launched June 23, 2021. Following a planned 5-week washout period, we began data capture on August 1, 2021, and the study period ended February 28, 2022. Data were queried from our EMR. We extracted ordering, laboratory, medication administration, and clinical data electronically and performed limited manual retrospective record reviews to assess fidelity, safety, and operational efficacy (manually extracted data were for quality management and validation and not part of data collection for our analyses).

Cohort assignment during SQuID was determined by medication orders and medication administration records (i.e., SQuID vs. traditional). Blood glucose checks were obtained from selected glucose lab results. Rescue dextrose administration was confirmed by medication administration records for any of several selected dextrose formulations in patients with glucose measurements of <70 mg/dL.

Outcome measures

Fidelity to the intervention was an important initial outcome for confirming implementation and effectiveness and assessing impacts of the intervention. This was evaluated by confirming that the number of blood glucose checks was appropriate for the patients EDLOS on a pathway that specifies glucose checks every 2 h, as timely blood glucose checks were previously noted to be a problem with the traditional pathway, and as dosing and timing of SQ insulin administration would follow upon blood glucose checks.

Safety of our intervention was evaluated by describing the frequency of hypoglycemic events requiring rescue dextrose using the SQuID pathway compared to use of a traditional insulin infusion. We provide these data for the patients with MTM-severity DKA treated on the traditional pathway during the concurrent study period as well for comparison.

Operational impacts were our primary outcome. We compared EDLOS for the SQuID cohort compared to the insulin infusion cohort in the postintervention period and to two historical control periods: the preintervention period and the pre-COVID period. To evaluate for any potential impacts of SQuID on ICU admission rate, we compared the proportion of patients with MTM-severity DKA in the postintervention period (SQuID + traditional) who were admitted to the ICU compared to the proportion of MTM-severity DKA patients admitted to the ICU in the historical control periods.

Sample size calculation

Sample size was directed at detection of a difference in our primary outcome measure, EDLOS among MTM-severity DKA patients not admitted to the ICU across cohorts. Using a one-sided Mann–Whitney U test, and given our sample sizes during the postintervention (n = 101 not admitted to an ICU, 73 on SQuID protocol and 28 traditional), preintervention (n = 88), and pre-COVID (n = 82) periods, we had 80%, power at an alpha = 0.05 to detect

differences in EDLOS (hours) of −2.9 h (traditional cohort during the study period), −1.9 (preintervention period), and −2.3 (pre-COVID period) compared to the SQuID cohort.

Analysis

Analysis was primarily descriptive. We present sociodemographic data for all MTM-severity DKA patients across cohorts. We present frequency of glucose checks per hour of EDLOS, proportion of patients requiring rescue dextrose for hypoglycemia, and EDLOS for MTM-severity DKA patients in the different cohorts not admitted to the ICU. We then evaluate the potential impact of SQuID on ICU utilization by comparing the proportion of MTM-severity DKA patients during the post-intervention period to that in the pre-intervention and pre-COVID periods. A schematic of this approach is provided in Figure 2B. We used a one-sided Mann–Whitney U-test to test for significant differences in EDLOS time distributions and chi-square or Fisher's exact test (as appropriate) for differences between proportions in ICU admissions. All primary outcomes are reported with 95% confidence intervals (CIs). Bootstrapping (n = 1000) was used to calculate 95% CIs for differences between medians. Missing data were classified as missing and noted in tables and outcomes. R version 4.0.2 (R Core Team, 2020) was used for all analyses and figures.

In addition to our main analyses, we did gather data to assess the prevailing average EDLOS during the study and control periods to help determine, in part, whether any changes observed may have been part of unmeasured secular trends. We tested for significant difference in mean monthly EDLOS times between the three groups using a one-way ANOVA and conducted a sensitivity analysis using quantile regression to control for monthly median EDLOS and number of ED visits during each time period. For the quantile regression model, we report coefficients with their respective 95% CIs.

RESULTS

During our 6-month study period, we identified 177 patients with MTM-severity DKA (78 SQuID, 99 traditional), of whom 76 were admitted to an ICU. Among those admitted to a medical floor, 73 patients were managed on the SQuID protocol and 28 were managed on an insulin infusion. A total of 27 DKA patients with prolonged boarding in the ED were treated on their respective protocols and were ultimately discharged home from the ED. For historical controls we identified 163 MTM-severity DKA patients in the preintervention period (88 non-ICU) and 161 patients in the pre-COVID period (82 non-ICU).

Details of comparison cohort descriptors, sociodemographics, and characteristics are provided in Table 1. Overall, patients on SQuID protocol were younger and more likely to be female, to have a lower acuity on the Emergency Severity Index,[28] and to be discharged from the ED. Summary statistics for all outcomes, stratified by group (SQuID, traditional, and historical controls), and differences for primary outcomes are in Table 2.

Fidelity

Overall, we found high fidelity for patients on SQuID pathway. Performance of blood glucose checks exceeded the q2-h testing requirement (median 1.0, interquartile range 0.8–1.1, range 0.3–1.6).

Safety

We found no differences in safety between the SQuID and traditional pathways. Rescue dextrose was administered to two patients on the protocol (2.7%) and one on the traditional pathway (3.6%) with no difference observed compared to MTM patients treated on the traditional pathway (difference in proportions −0.9).

Operational impact: EDLOS

Median EDLOS was significantly shorter for the SQuID cohort, compared to the traditional cohort during the postintervention (−3.0, 95% confidence interval [CI] −8.5 to −1.4), the preintervention (−1.4, 95% CI −3.1 to −0.1), and the pre-COVID (−3.6, 95% CI −7.5 to −1.8) periods (Figure 3).

Operational impact: ICU admissions

When comparing ICU admissions for all MTM-severity DKA patients in the postintervention period (42.9%) compared to the preintervention (46.0%) and pre-COVID control periods (49.1%), we observed reductions of −3.1% (95% CI −14.2 to 8.1) and − 6.2% (95% CI −17.3 to 5.1), respectively, but these differences did not achieve significance.

Prevailing EDLOS Data

We examined monthly EDLOS time for all visits during the SQuID intervention (mean ± SD 5.9 ± 0.4, n = 45,936), preintervention (mean ± SD 5.6 ± 0.3, n = 43,827), and pre-COVID (mean ± SD 6.0 ± 0.3, n = 52,017) periods. Mean monthly EDLOS times were not significantly different between the three time periods (F = 1.8, p = 0.187). The sensitivity analysis did not change the significance of our findings. Traditional, pre-SQuID, and pre-COVID EDLOS times were significantly higher than SQuID EDLOS in the unadjusted quantile regression model (2.2, 95% CI 1.6–6.4; 1.4, 95% CI 0.7–2.8; and 3.7, 95% CI 2.6–6.4, respectively) and the quantile regression model adjusting for monthly median (all ED visits during each time period) EDLOS and number of ED visits

TABLE 1 Demographics and clinical characteristics of patients with MTM-severity DKA by group (SQuID, traditional, preintervention, and pre-COVID).

	Post-intervention		Historical controls	
	SQuID ($n = 78$)	Traditional ($n = 99$)	Pre-intervention ($n = 163$)	Pre-COVID ($n = 161$)
Age (years)	41.5 (30.3–52.0)	55.0 (40.5–66.5)	49.0 (30.5–61.0)	48.0 (31.0–61.0)
Sex				
Male	32 (41.0)	57 (57.6)	97 (59.5)	98 (60.9)
Female	46 (59.0)	42 (42.4)	66 (40.5)	63 (39.1)
Race				
Black or African American	62 (79.5)	77 (77.8)	109 (66.9)	118 (73.3)
White or Caucasian	15 (19.2)	19 (19.2)	49 (30.1)	43 (26.7)
ESI				
1	0 (0.0)	4 (4.0)	5 (3.1)	2 (1.2)
2	55 (70.5)	72 (72.7)	125 (76.7)	127 (78.9)
3	23 (29.5)	22 (22.2)	31 (19.0)	31 (19.3)
4	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)
5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0 (0.0)	1 (1.0)	0 (0.0)	1 (0.6)
ED disposition				
Admit	69 (88.5)	93 (93.9)	146 (89.6)	133 (82.6)
Discharge	9 (11.5)	0 (0.0)	8 (4.9)	10 (6.2)
Other	0 (0.0)	6 (6.1)	9 (5.5)	18 (11.2)

Note: Data are reported as median (IQR) or *n* (%).

Abbreviations: DKA, diabetic ketoacidosis; ESI, Emergency Severity Index; MTM, mild to moderate; SQuID, subcutaneous insulin in diabetic ketoacidosis.

TABLE 2 Outcomes by treatment group during postintervention (SQuID and traditional), preintervention, and pre-COVID controls.

	Postintervention		Historical controls	
	SQuID and traditional		Preintervention	Pre-COVID
Patients with MTM-severity DKA	$n = 177$		$n = 163$	$n = 161$
Admitted to ICU	76 (42.9)		75 (46.0) [−3.1][a]	79 (49.1) [−6.2][a]
Non-ICU patients	$n = 101$		$n = 88$	$n = 82$
	SQuID ($n = 73$)	Traditional ($n = 28$)		
Glucose tests/hour	1.0 (0.8–1.1)	1.0 (0.8–1.1)	1.0 (0.9–1.2) [0.0][a]	1.0 (0.8–1.1) [0.0][a]
Rescue dextrose	2 (2.7)	1 (3.6)	2 (2.3) [0.4][a]	0 (0.0) [2.7][a]
EDLOS (h)	8.9 (6.5–11.5)	11.9 (9.6–18.6)	10.3 (7.7–12.9) [−1.4][b]	12.5 (8.7–19.3) [−3.6][b]

Note: Data are reported as *n* (%) or median (IQR).

Abbreviations: DKA, diabetic ketoacidosis; EDLOS, emergency department length of stay; ICU, intensive care unit; MTM, mild to moderate; SQuID, subcutaneous insulin in diabetic ketoacidosis.

[a]Numbers in brackets are differences between patients on SQuID protocol and historical control cohorts.

[b]Difference was significant.

(3.0, 95% CI 1.5–6.6; 1.8, 95% CI 0.8–3.2; and 3.4, 95% CI 1.8–6.0, respectively). Neither monthly median EDLOS nor monthly median number of ED visits were significant in the quantile regression model (0.0, 95% CI 0.0–0.0; and 0.0, 95% CI 0.0–0.1, respectively).

DISCUSSION

In this study, we found that a SQ fast-acting insulin protocol is an excellent option for MTM-severity DKA patients in the ED, reducing EDLOS and holding the potential for reductions in ICU admissions

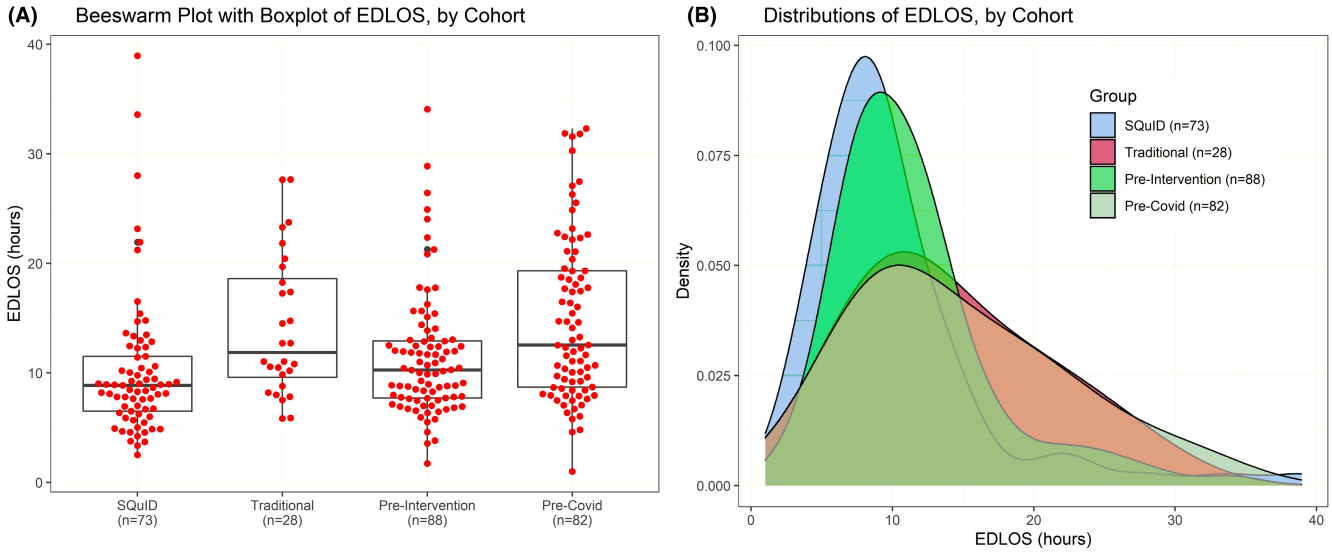

FIGURE 3 (A) Beeswarm plot with boxplot of EDLOS, by cohort. (B) Distributions of EDLOS, by cohort. EDLOS, emergency department length of stay; SQuID, subcutaneous insulin in diabetic ketoacidosis.

for MTM DKA. We observed excellent performance on our metric for fidelity to the protocol and had equivalent safety compared to a traditional insulin infusion pathway. Our project was met with a high degree of enthusiasm by ED providers and by the inpatient teams, leading to a forthcoming expansion of the SQuID protocol to a general medical floor and liberalization of criteria to include more complex patients. We anticipate this will result in a greater impact on reducing ICU admissions for DKA. This study adds to literature demonstrating efficacy of SQ insulin for this purpose and suggests that this might be a useful strategy for patient throughput in facilities where lack of ICU or intermediate care bed availability result in patient delays and prolonged EDLOS.

A combination of factors facilitated hospital approval of this protocol for treatment of DKA outside an ICU setting. These included a concurrent overall hospital goal of improving glycemic control (hyper- and hypoglycemic episodes), burgeoning data on the safety and efficacy of SQ insulin for DKA, limited ICU availability for DKA patients, prolonged EDLOS for DKA patients treated in the ED, and multidisciplinary interest in pursuing an alternate approach. Because efficacy and safety of SQ insulin pathways have been previously demonstrated, we were able to launch this protocol as a standard of care while primarily evaluating its impact on operational metrics.

Our main findings are not particularly surprising. Our protocol targets lower severity DKA patients and avoids the requirements for anion gap closure in the ED and use of an IV infusion that must be discontinued prior to admission to a medical floor. Though both groups being compared (SQuID vs. traditional) are MTM in DKA severity, they are, by definition, not equivalent. This is driven by the fact that the dedicated floor for SQuID was an inpatient observation unit where a maximum HLOS limits the complexity of patients who can be treated there. While this is very likely to impact differences in HLOS (we did not measure these), differences in EDLOS are more likely to be attributable to the protocol and to lengthy times a patient must remain on an IV infusion in the ED until glycemic control and anion gap closure. This is also what likely drives the failure to observe a significant reduction in ICU admission rate among MTM-severity DKA patients, due to the exclusion of moderate-severity DKA patients who might otherwise have been candidates for an ICU bed.

Many issues impact EDLOS and ICU admission determinations and these are likely to vary across institutions. Bed availability issues and boarding have the potential to significantly blunt effect sizes in either direction. In addition, there were many unanticipated impacts of COVID-19 on our study. All admitted patients are required to have COVID testing with results prior to bed assignment. At times this could have been initiated late, or the test ordered may not have matched the hospital requirements, which could result in ordering a batched rather than concurrent testing. More significantly, ED visit volumes were notably reduced after the first wave of COVID, impacting the number of DKA patients we treated. Moreover, the dedicated floor for SQuID patients was unavailable to us for periods during the pandemic, when it was at times used as a COVID isolation floor. While ICU beds for a patient with DKA were very limited early in the pandemic, at other times these were much easier to obtain than usual. Apart from the impacts of COVID are the routine delays, ebbs, and flows in either hospital bed or ICU bed availability. Such vagaries are challenging to control for. Early on we did observe an impact on ICU admission rate, but this became nonsignificant over a broader window of time.

During our washout period and extending somewhat beyond, we did encounter several issues that required adjustment and education. These included cases of misclassification, whereby patients who were in severe DKA or who clearly had exclusion criteria for SQuID were nevertheless started on the SQ insulin protocol. This was usually recognized in the ED in near real time and these patients

were removed from the protocol. We also had a few cases of underdosing or delayed administration of long-acting insulin after patient arrival on the medical floor, resulting in recurrence of hyperglycemia. Another issue identified related to failure to initiate dextrose-containing fluids in a timely fashion. This occurred both in the ED and on the floor and was responsible for at least one of the cases requiring rescue dextrose. For the handful of patients on the SQuID protocol who did develop recurrence of hyperglycemia or an anion gap, our default protocol was to switch them to an insulin infusion, which then required them to go to an ICU. It was subsequently determined that if these patients remain in MTM-severity DKA, they can and should generally just be restarted on the SQuID protocol and that admission to an ICU is unnecessary. In response to some of these issues we made some changes to our order set including adding a BPA for the timing of dextrose-containing fluid and modifying our dextrose-containing fluid order to be titratable.

While it has been proposed that care of DKA might be best suited for an intermediate care unit rather than an ICU, not all hospitals have these units, which is the case in our facility. Even in facilities with these units, those beds are increasingly in demand, making a protocol that can deployed on a medical floor compelling. Future areas of research may include assessing patient and staff satisfaction with this protocol as has been suggested by other researchers,[26] assessing safety and training requirements for expansion of the protocol beyond cohorted areas in the hospital, evaluating factors that might aid in prevention of DKA, and resource development for wider dissemination.

LIMITATIONS

This is a single-center study in a busy Level 1 academic urban trauma center with related potential limitations in generalizability. However, ED boarding is widespread, limited ICU availability is commonplace, and diabetes and DKA are highly prevalent. This study was likely more difficult to carry out in this setting with many competing time-critical conditions and might be easier to operationalize in lower volume EDs and nonreferral centers. Findings related to reductions in boarding and ICU admissions might not be reproducible in settings where DKA patients are easily admitted to the ICU rather than being routinely managed in the ED or where intermediate care beds are available that allow insulin infusions. Though our data extraction was performed retrospectively we do not feel there are significant limitations in the validity or accuracy of our findings as confirmed in manual quality checks. As noted in the Discussion, the study protocol exclusion criteria essentially guarantee that the distribution of patients in our two cohorts of interest are necessarily different in complexity. This was unavoidable as a practical matter since it was important for success of the launch of this effort to select lower severity patients with this new protocol in a non-ICU setting. However, we do not feel differences between the SQuID and traditional cohorts significantly impacted EDLOS compared to the impacts of the respective protocols. We considered use of an interrupted time-series design, but our observed numbers were much lower than anticipated, in large part due to the COVID pandemic. Our use of preintervention and historical control cohorts attempt to provide some information on prevailing secular trends. At times during the study period the dedicated floor for SQuID patients was used as a COVID floor so that it was unavailable for our purposes. At other times this dedicated floor was full, in part due to shifts in bed availability elsewhere, again related to COVID. Our use of frequency of fingerstick blood glucose to assess fidelity assesses only one aspect of the treatment protocol. In limited manual reviews performed for other purposes we did identify examples of problems with the timeliness and initiation of dextrose-containing fluids and one medication error in administering Lispro. Safety (frequency of adverse events) was a secondary outcome in our study and though we did not find a difference between SQuID and the traditional pathways, our study was not powered to detect adverse events with high sensitivity and specificity, which generally requires very large numbers.

CONCLUSIONS

In this single academic medical center study, subcutaneous fast-acting insulin analogs for the treatment of mild to moderate–severity diabetic ketoacidosis in the ED was effective, demonstrated equivalent safety, and reduced ED length of stay.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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