



Comparison of outcomes and costs between adult diabetic ketoacidosis patients admitted to the ICU and step-down unit

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ABSTRACT

Purpose: There is wide variation in the utilization of Intensive Care Unit (ICU) beds for treatment and monitoring of adult patients with Diabetic Ketoacidosis (DKA). We sought to compare the outcomes and hospital costs of adult DKA patients admitted to ICUs as compared to those admitted to step-down units.

Materials and methods: We included consecutive adult patients from two hospitals with a diagnosis of DKA. Patients were either admitted to the ICU, or a step-down unit, which has a nurse-to-patient ratio of 2:1, but does not have capability for mechanical ventilation or administration of vasoactive agents. The primary outcome was in-hospital mortality.

Results: We included 872 patients in the analysis. 71 (8.1%) were admitted to ICU, while 801 (91.9%) were admitted to a step-down unit. We found no difference in in-hospital mortality between patients admitted to the ICU and those admitted to the step-down unit (adjusted odds ratio [OR]: 1.14, 95% confidence interval [CI]: 0.87–2.64). Mean total hospital costs were significantly higher for patients admitted to the ICU (\$20,428 vs. \$6484, $P < 0.001$).

Conclusions: Adult DKA patients admitted to a step-down unit had comparable in-hospital mortality and lower hospital costs as compared to those admitted to the ICU.

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1. Introduction

Diabetes mellitus (DM) is a disease associated with significant morbidity and mortality, and patients with DM account for significant healthcare spending [1]. These costs appear to be increasing each year, with a noted increasing number of hospitalizations in North America for DM and diabetic ketoacidosis (DKA) [2]. DKA is an acute metabolic disorder, which is primarily characterized by an increased presence of circulating ketone bodies, and the development of severe ketoacidosis

in the presence of prolonged uncontrolled hyperglycemia, usually secondary to insulin deficiency [3,4]. DKA is more commonly seen in patients with insulin-dependent DM, particularly children and young adults. Prior to the discovery of insulin, mortality from DKA exceeded 90%; however, contemporary management utilizing standardized protocols for resuscitation, insulin delivery, and monitoring has resulted in significant improvement in patient outcomes [5,6]. The American Diabetes Association (ADA) has recommended that adult patients with severe DKA be treated and monitored in an Intensive Care Unit (ICU) setting, in order to maintain close monitoring during provision of care [3,7].

Recent evidence has demonstrated wide variation in the utilization of ICU beds for the care of DKA patients [8]. In some centres, all patients

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diagnosed with DKA are routinely admitted to the ICU to facilitate close monitoring, frequent blood work, and medication infusions (e.g. insulin), that are not easily administered on the hospital wards. However, in other centres, as little as 2% of DKA patients are admitted to the ICU, with the remainder managed in specialized step-down units [8]. These intermediate care units are usually not capable of providing advanced life support such as invasive mechanical ventilation or vasoactive medications, but do allow for non-invasive ventilation, telemetry, and lower patient-to-nursing ratios for closer provision of care [9]. Little is known regarding the associated outcomes and cost-effectiveness of these units (as compared with care in ICU settings) in DKA patients [10]. Given the growing shortage of ICU capacity [11], and the potential impact this may have on patient outcomes [12,13], a greater understanding about the safety of step-down units in the care of DKA patients is necessary. We sought to compare the outcomes and costs of adult patients with DKA admitted to ICU as compared to those admitted to step-down units.

2. Materials and methods

Ethics approval for this study was obtained from The Ottawa Health Science Network Research Ethics Board.

2.1. Study design, setting and subjects

We studied patients at two tertiary-level academic hospitals within The Ottawa Hospital network (Ottawa, ON). This combined network has 1163 beds, and handles over 160,000 emergency department encounters annually. Both hospitals have a mixed medical-surgical ICU, each with 28 ICU beds, and approximately 2500 combined ICU admissions per year. Since the management of patients with a diagnosis of DKA requires close nursing care (due to infusions of insulin and fluids, as well as frequent bloodwork), patients who are not admitted to the ICU are admitted to an intermediate care, step-down unit. This step-down unit, comprised of 6 beds at each hospital, is managed by the General Internal Medicine service. The nurse-to-patient ratio is 2:1 (as opposed to 1:1 in the ICU), and all patients are admitted with cardiac telemetry. While this step-down unit is able to provide the high degree of nursing care associated with the management of DKA, and can provide non-invasive ventilation, it does not have capability to provide invasive ventilation, arterial monitoring, or vasoactive medications, which are available in the ICU. Decisions related to ICU or step-down disposition, transfer, or discharge are collaboratively made by both ICU and General Internal Medicine medical teams. The included hospitals did not utilize a protocol for monitoring and management of DKA during the study period. Regardless of the unit of admission, patient education was evaluated and reinforced over the course of hospitalization.

We retrospectively analyzed prospectively-collected data stored between 2011 and 2016 from The Ottawa Hospital Data Warehouse, a health administrative database that has been widely used in previous health services research [14–18]. Data quality assessments were performed during development, and are executed routinely as new data are included to ensure completeness and accuracy. We did not include variables that did not have complete data for all study patients. We included all adult patients (≥ 18 years of age) that had a primary hospital admission or discharge diagnosis of DKA. The criteria for diagnosis of DKA were adapted from the ADA [7] (and based on initial laboratory values), which defines DKA by presence of all of the following: a) Serum glucose >13.9 mmol/L; b) Presence of ketonuria or ketonemia; c) Arterial pH <7.30 ; and d) Serum bicarbonate <18 mmol/L. If arterial pH was not available, we instead used venous pH. Resolution of DKA was also defined using the existing ADA criteria, which includes all of the following: a) Serum glucose <11.1 mmol/L; b) Venous pH >7.30 ; and c) Serum bicarbonate >18 mmol/L. We excluded all patients requiring invasive mechanical ventilation or vasoactive medications, as these patients could not be managed in the step-down unit at our centre.

2.2. Data collection

We obtained all data from The Ottawa Hospital Data Warehouse. For each patient, we abstracted basic demographic data, comorbidities, and Elixhauser Comorbidity Score [19]. Data are collected by clerical staff at patient arrival, and include initial vital signs, and laboratory values. Illness severity was quantified using the Multiple Organ Dysfunction Score (MODS) [20]. Data were collected from hospital admission until hospital discharge, or in-hospital death. This included ICU length of stay (LOS), hospital LOS, and final disposition status.

Patient costs were determined using the case-costing system of The Ottawa Hospital Data Warehouse, as utilized previously [15,16]. Total hospital costs include both direct and indirect costs from a hospital perspective. ‘Direct’ costs refer to all hospital expenses with fee codes linked to the patient chart. These ‘Direct’ costs also include salaries and benefits for unit producing and management staff, equipment, and screening and procedure materials, but do not include physician costs. Indirect costs refer to any overhead operational fees associated with the service being provided to the patient, such as the cost of the room they occupy. Cost per survivor is calculated by dividing total costs by the number of patients surviving to hospital discharge. The Ottawa Hospital uses a standardized case-costing methodology that was developed by the Ontario Case Costing Initiative, and is based on the Canadian Institute for Health Information Management guidelines [21]. Costs were then indexed to 2018 Canadian Dollars using consumer price indices, as described previously [15,22,23].

The primary outcome was in-hospital mortality. Secondary outcomes included ICU LOS, total hospital LOS, total hospital costs, hospital cost per day, and hospital cost per survivor.

2.3. Statistical analysis

All statistical analyses were performed with commercially available statistical packages (R, Version 3.3.3 and IBM SPSS, Version 24.0). Data are presented as either mean values, with standard deviation (SD), or medians, with interquartile range (IQR). The Student’s *t*-test (parametric values), Mann-Whitney test (for non-parametric values), and χ^2 (for categorical values) were used to determine between-group differences. In evaluating the outcome of in-hospital mortality, we used multivariable logistic regression modeling to adjust for potential confounders, including patient age, sex, illness severity (by MODS), and Elixhauser Comorbidity Score. We assessed variation in total hospital costs using a multivariable generalized linear model with a gamma distribution and a log link function to estimate cost coefficients and 95% confidence intervals (CI). Generalized linear models are the recommended methodology for modeling the impact of covariates in cost analyses of health services, as they can account for significant skew without the need for transformation [24,25]. A *P* value of ≤ 0.05 was considered statistically significant.

3. Results

From 2011 to 2016, 950 patients were admitted to hospital with a diagnosis of DKA. From these, we excluded 78 from the analysis, as 67 of these patients (7.1%) did not meet ADA criteria, and 11 patients (1.2%) required mechanical ventilation or vasoactive medications. We ultimately included 872 patients in the analysis. Of these, 71 patients (8.1%) were admitted to the ICU, while the remaining 801 (91.9%) were admitted to the step-down unit. Baseline characteristics of ICU and step-down unit patients are displayed in Table 1. No differences were seen between groups with regards to age, sex, baseline comorbidities, or illness severity (by MODS). The majority of patients in the cohort had Type 1 DM (81.6% of ICU patients vs. 78.7% of step-down patients, *P* = 0.55). When comparing chronic complications of DM between groups, no statistically significant differences were found. The large majority of patients in both groups had been managed on

Table 1

– Baseline characteristics of entire cohort: Abbreviations: DKA = Diabetic Ketoacidosis; DM = Diabetes Mellitus; ICU = Intensive Care Unit; IQR = Interquartile Range; SD = Standard Deviation.

	DKA ICU patients (n = 71)	DKA step-down patients (n = 801)	P-Value
Age, years, mean (range)	42.2 (18.7)	44.1 (19.6)	0.53
Male, n (%)	36 (50.7)	404 (50.4)	
Comorbidities, n (%)			
Congestive heart failure	0 (0)	11 (1.4)	0.32
Arrhythmia	3 (4.2)	24 (3.0)	0.48
Valvular disease	0 (0)	3 (0.3)	0.99
Hypertension	15 (21.1)	163 (20.3)	0.87
Chronic obstructive pulmonary disease	2 (2.8)	17 (2.1)	0.70
Liver disease	1 (1.4)	18 (2.2)	0.64
Metastatic cancer	2 (2.8)	24 (3.0)	0.93
Elixhauser comorbidity score, mean (SD)	1.8 (0.8)	1.5 (0.8)	0.43
Multiple organ dysfunction score, median (IQR)	2 (0–2)	2 (0–2)	0.31
DM diagnosis			0.55
Type I DM	58 (81.6)	630 (78.7)	
Type II DM	13 (18.3)	171 (21.3)	
New DM diagnosis	6 (8.4)	63 (7.9)	0.86
DM complications, n (%)			
Nephropathy	9 (12.7)	112 (14.0)	0.76
Retinopathy	8 (11.2)	98 (12.2)	0.81
Neuropathy	10 (14.1)	120 (15.0)	0.84
Peripheral vascular disease	5 (7.0)	69 (8.6)	0.65
Gastroparesis	3 (4.2)	38 (4.7)	0.67
Coronary artery disease	8 (11.3)	99 (12.4)	0.51
Severe DKA, n (%)	3 (4.2)	7 (0.9)	<0.01
Medications before DKA episode, n (%)			0.90
Insulin	60 (84.5)	670 (83.6)	
Oral hypoglycemic agent	5 (7.0)	68 (8.5)	
No therapy	6 (11.3)	63 (7.9)	
Precipitant for DKA, n (%)			0.91
Medication non-compliance	53 (74.6)	600 (74.9)	
Infection	7 (9.9)	74 (9.2)	
New diagnosis	6 (8.4)	63 (7.9)	
Unknown	4 (5.6)	46 (5.7)	
Ethanol abuse	1 (1.4)	18 (2.2)	

subcutaneous insulin injections prior to hospital presentation (84.5% of ICU patients vs. 83.6% of step-down patients, $P = 0.90$). The primary precipitant in both groups was determined to be medication non-compliance (74.6% of ICU patients vs. 74.9% of step-down patients,

$P = 0.91$). Patient vital signs and laboratory values at the time of hospital arrival are demonstrated in Table 2. No differences in initial vital signs at hospital presentation were found between groups. Similarly, no statistically significant differences in initial laboratory values were found, including initial blood glucose, anion gap, venous pH, or serum bicarbonate.

Outcomes of ICU and step-down unit DKA patients are displayed in Table 3. Six ICU patients (8.4%) died in-hospital, as compared to 62 step-down unit patients (7.7%). The multivariable logistic regression model for mortality is depicted in Supplementary Table 1. After controlling for confounders, no significant difference in in-hospital mortality was found between groups (adjusted OR, 1.14; 95% CI: 0.87–2.64). Median hospital length of stay was significantly longer among DKA patients admitted to the ICU (9.0 days vs. 5.0 days, $P < 0.001$). No significant difference in median time to resolution of DKA was found between groups ($P = 0.32$). Additionally, subgroup analysis only examining patients presenting to hospital from home found no difference in the proportion of patients discharged to long-term care facilities (5.6% of ICU patients vs. 7.6% of step-down patients, $P = 0.59$).

Finally, we examined the total hospital costs of ICU compared to step-down DKA patients (Table 4). Total hospital costs were significantly higher among ICU patients (\$20,716 vs. \$6484, $P < 0.001$). When comparing contributors to total costs, ICU patients had significantly higher costs for laboratory tests, imaging, and pharmaceutical resources, however, no significant differences were seen in costs of food services, health professional services (non-physician), and nursing. Differences in total hospital cost between ICU and step-down patients were also evident using the generalized linear model (Supplementary Table 2), where disposition to ICU was an independent predictor of overall costs ($\beta = 2.26$; 95% CI: 2.04–2.54, $P < 0.001$).

4. Discussion

We found that DKA patients admitted to a step-down unit had significantly lower total hospital costs, with no difference in in-hospital mortality or discharge destination. These findings lend support to the utilization and cost effectiveness of step-down units in the care of this patient population.

Previously, a diagnosis of DKA was fatal in the large majority of cases. The advent of insulin therapy has now completely changed the outlook for these patients, and protocolized care has substantially improved outcomes associated with DKA [5,6]. While outcomes have improved, the cost of significant nursing workload and resource utilization have

Table 2

– Vital signs and laboratory values of entire cohort upon hospital arrival: Abbreviations: DKA = Diabetic Ketoacidosis; ICU = Intensive Care Unit; IQR = Interquartile Range; SD = Standard Deviation.

	DKA ICU patients (n = 71)	DKA step-down patients (n = 801)	P-Value
Vital signs on arrival			
Systolic blood pressure, mmHg, mean (SD)	138.1 (28.4)	134.2 (26.5)	0.31
Diastolic blood pressure, mmHg, mean (SD)	72.3 (12.7)	71.7 (11.2)	0.53
Mean arterial pressure, mmHg, mean (SD)	93.4 (16.1)	92.6 (15.2)	0.47
Heart rate, beats/min, mean (SD)	104.8 (28.4)	102.4 (27.3)	0.27
Temperature, degrees Celsius, mean (SD)	36.9 (0.8)	36.8 (0.8)	0.74
Oxygen saturation, %, mean (SD)	94.6 (4.4)	95.3 (3.8)	0.35
Glasgow coma scale <15, n (%)	11 (15.5)	136 (17.0)	0.75
Laboratory values on arrival			
Blood glucose, mmol/L, mean (SD)	28.4 (10.7)	26.7 (10.2)	0.23
Anion gap, mEq/L, median (IQR)	20 (15–24)	20 (13–23)	0.35
Venous pH, median (IQR)	7.11 (7.05–7.19)	7.13 (7.07–7.25)	0.18
Bicarbonate, mmol/L, median (IQR)	8 (4–14)	10 (5–17)	0.31
Beta-hydroxybutyrate, mmol/L, median (IQR)	6.4 (3.4–8.6)	6.1 (3.0–8.4)	0.22
Sodium, mmol/L, mean (SD)	128.5 (5.3)	129.2 (4.7)	0.43
Potassium, mmol/L, mean (SD)	4.1 (0.7)	4.0 (0.6)	0.74
Creatinine, μ mol/L, median (IQR)	94 (66–145)	96 (71–150)	0.29
Urea, mmol/L, median (IQR)	2.4 (1.6–3.1)	2.6 (1.6–3.5)	0.33
Albumin, g/L, mean (SD)	24.7 (6.7)	25.3 (6.2)	0.64
Lactate, mmol/L, median (IQR)	3.1 (1.9–4.5)	2.8 (1.6–4.1)	0.28

Table 3

– Patient outcomes: Abbreviations: DKA = Diabetic Ketoacidosis; ICU = Intensive Care Unit; IQR = Interquartile Range; LOS = Length of Stay; SD = Standard Deviation.

	DKA ICU patients (n = 71)	DKA step-down patients (n = 801)	P-Value
In-Hospital Mortality, n (%)	6 (8.4)	62 (7.7)	0.83
ICU LOS, days, median (IQR)	4.0 (3.0–5.3)	–	
Hospital LOS, days, median (IQR)	9.0 (5.8–13.0)	5.0 (2.0–6.8)	<0.001
Disposition, n (%)			0.59
Home	50 (94.3)	576 (92.3)	
Long-term care facility	3 (5.6)	48 (7.6)	
Time to resolution of DKA, days, median (IQR)	1 (0.3–1.5)	1 (0.2–1.2)	0.32

similarly increased [26]. For this reason, existing practice guidelines from the ADA have recommended monitoring of these patients (especially those with severe disease) in an ICU setting [3,7]. In many centres, all DKA patients are admitted to the ICU, regardless of the severity of their illness [27], although there is significant variation in this practice across North America [8]. Uniform admission of these patients, many with lower acuity illness, may contribute to strained ICU capacity, which has been associated with worse outcomes among critically ill patients [12,13]. Therefore, evaluating the cost-effectiveness of step-down units presents an important avenue for mitigating ICU strain and improving efficiency of resource utilization.

We found no difference in overall mortality among patients admitted to the ICU, and those admitted to a step-down unit. The mortality seen in our cohort was low, and is consistent with what has been seen in previous investigations of this population, particularly in Canada [28]. There was no difference in time to resolution of DKA between ICU patients and step-down patients. Previous work has demonstrated that only patients with severe acidosis (with resultant hemodynamic instability) and decreased level of consciousness seem to benefit from ICU admission [29]. Taken together, this suggests that DKA patients not requiring critical care interventions (namely mechanical ventilation and vasoactive medications) can be safely managed in a step-down unit.

Unsurprisingly, we found that DKA patients admitted to the ICU had higher costs than those admitted to the step-down unit. Overall hospital length of stay was longer among the ICU patients, despite no difference between groups in time to DKA resolution, and this is a significant driver of overall costs [30,31]. This is likely due to ICU patients waiting for transfer to the ward. The ICU itself is a particularly resource-intensive unit, and can account for a significant proportion of hospital costs [30,31]. In addition, ICU demands are expected to increase in the coming decade [32]. Therefore, it is important to ensure that patients admitted to the ICU are going to benefit from the care provided to a greater degree than other areas of the hospital, to justify the increased costs. Our findings show significantly increased costs among ICU DKA patients, without any obvious benefit in patient outcomes. Therefore, hospitals

should consider admitting such patients (who do not require critical care interventions) to an intermediate care unit.

Our study has several strengths, including uniform criteria for patient inclusion, granular characteristic data, and adjustment for confounding variables. There are, however, some limitations that hinder the generalizability of our results. Importantly, despite the fact that there were no obvious baseline differences between the groups, there were still an appreciable number of patients admitted to the ICU. Although a few possible explanations for this exist, the most likely is step-down capacity. With only six beds at each hospital, these units are quickly filled. As a result, patients requiring such close monitoring would have no alternative other than the ICU. A second limitation relates to data collection. While data were collected prospectively, they were not collected specifically for this study, and were analyzed retrospectively. This can raise questions related to validity and reliability. Future prospective work is necessary in this area, and prospective data collection may prove valuable in the creation of decision instruments for risk-stratification of patients with DKA. Additionally, our study was an observational study, and as such was not powered to detect a difference in mortality. It is possible that, on a larger scale, there is a mortality benefit to ICU care of DKA patients, however this has not been demonstrated in previous studies [8,33,34]. Although our data were gathered from two different hospitals, they exist within the same healthcare system and city. Given the known regional variation in ICU admission criteria, and the level of care that can be provided in ICUs or step-down units, the generalizability of the results may be limited. However, the mortality seen in our population is similar to that reported in other studies worldwide [27,28]. That said, individual centres must evaluate their current practices of admission among this patient population, and independently determine the benefits of instituting such step-down units. Step-down units must be safe, provide high quality of care to patients, and ideally be cost-effective. This may not be equally feasible in all centres. Finally, we only evaluated in-hospital mortality, and did not examine long-term mortality, which has been shown to be elevated in DKA patients [28]. It is possible that these patients suffered downstream complications, or were readmitted to other ICUs in the following months.

5. Conclusion

We found that DKA patients admitted to a step-down unit had comparable outcomes and significantly lower hospital costs than those admitted to the ICU. Healthcare providers should weigh the possible benefits from critical care interventions in this population prior to admission. Given the demonstrated favourable economic implications of step-down units in the care of DKA patients, hospitals should consider the creation of such intermediate units to increase efficiency of resource utilization.

Table 4

– Costs: All costs in Canadian dollars. Abbreviations: DKA = Diabetic Ketoacidosis; ICU = Intensive Care Unit; SD = Standard Deviation.

	DKA ICU patients (n = 71)	DKA step-down patients (n = 801)	P-Value
Total costs, \$, mean (SD)	20,716 (14163)	6484 (5734)	<0.001
Total direct costs, \$, mean (SD)	15,699 (10759)	4772 (3473)	<0.01
Total cost/day, \$, mean (SD)	2955 (2649)	1841 (1638)	<0.01
Cost/survivor, \$, mean (SD)	22,628 (15895)	7028 (6215)	<0.001
Specific costs, \$, mean (SD)			
Food services	400 (187)	248 (149)	0.18
ICU	7188 (4292)	–	
Laboratory tests	1090 (726)	542 (498)	<0.001
Imaging	746 (418)	345 (257)	<0.01
Pharmacy	1173 (452)	600 (489)	<0.01
Health professional services	1035 (282)	1158 (723)	0.41
Nursing	5394 (2256)	4714 (1456)	0.08

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcrc.2018.12.014>.

Conflicts of interest

None.

Author contributions

SMF, SMB, BR, DIM, and KK designed the study. SMF and KK gathered the data. SMF, SMB, BR, DIM, and KK analyzed the data. SMF, SMB, BR, DIM, KT, AJF, AT, PMR, ER, PT, and KK wrote the manuscript and agree to be responsible for its contents.

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