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# Management of diabetic keto-acidosis in adult patients admitted to intensive care unit: an ESICM-endorsed international survey

Mathieu Jozwiak <sup>1 2</sup>, Margaret M Hayes <sup>3</sup>, Emmanuel Canet <sup>4</sup>, Alexandre Lautrette <sup>5</sup>, Maël-Morvan Duroyon <sup>6</sup>, Nicolas Molinari <sup>6</sup>, Boris Jung <sup>7</sup>

<sup>1</sup> Service de Médecine Intensive-Réanimation, CHU de Nice Hôpital L'Archet 1, 151 Route Saint Antoine de Ginestière, 06200, Nice, France. [jozwiak.m@chu-nice.fr](mailto:jozwiak.m@chu-nice.fr).

<sup>2</sup> Equipe 2 CARRES, UR2CA - Unité de Recherche Clinique Côte d'Azur, Université Côte d'Azur, Nice, France. [jozwiak.m@chu-nice.fr](mailto:jozwiak.m@chu-nice.fr).

<sup>3</sup> Division of Pulmonary, Critical Care and Sleep Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA.

<sup>4</sup> Service de Médecine Intensive-Réanimation, CHU de Nantes, Nantes, France.

<sup>5</sup> Service de Réanimation, Centre Jean Perrin, Clermont Ferrand, France.

<sup>6</sup> Department of Statistics, IMAG, CNRS, Univ Montpellier, CHU Montpellier, 34000, Montpellier, France.

<sup>7</sup> Service de Médecine Intensive-Réanimation, CHU de Montpellier, Université de Montpellier, INSERM CNRS PhyMedExp, Montpellier, France.

## Trial registration

Not applicable.

## Keywords:

Balanced solution; DKA management; Diabetic keto-acidosis; Fluid resuscitation; Insulin therapy; Isotonic saline; Sodium bicarbonate.

## \*Correspondence:

Mathieu Jozwiak

[jozwiak.m@chu-nice.fr](mailto:jozwiak.m@chu-nice.fr)

# Abstract

## Background:

Guidelines for diabetic ketoacidosis (DKA) management are limited, resulting in varied practices. This study assessed Intensive Care Unit (ICU) admission criteria, fluid resuscitation, insulin therapy, and metabolic management in adult patients with DKA.

## Methods:

An international survey of ICU clinicians consisted of 39 items that focused on management of DKA and was endorsed by the European Society of the Intensive Care Medicine. An experienced ICU was defined as a unit admitting > 20 patients with DKA per year.

## Results:

A total of 522 respondents from 57 different countries participated: 295(57%) worked in Europe, 86(16%) in North America, 25(5%) in South America, 52(10%) in Africa, 52(10%) in Asia and 12(2%) in Oceania. Among respondents, 377(72%) worked in teaching hospitals, 355(68%) in medical-surgical ICUs, and 204(39%) in experienced ICUs. The pH value (< 7.20), arterial or venous bicarbonate concentration (< 15 mmol/L), and the need for continuous intravenous insulin (regardless of the dose) were considered criteria for ICU admission by 362(69%), 240(46%) and 264(51%) respondents, respectively. A protocol for fluid resuscitation was available for 290(63%) respondents, 135(29%) administered isotonic saline only, 173(38%) administered balanced solutions only, and 153(33%) administered both. A protocol for insulin therapy was available for 355(77%) respondents. An initial bolus of intravenous insulin was administered by 228(49%) respondents, 221(48%) used an initial continuous intravenous insulin dose of 0.1 UI/kg/h, 42(9%) used an initial predefined fixed dose, 159(35%) based the initial dose on blood glucose and 39(8%) on blood and/or urine ketones. Fluid choice and modalities of intravenous insulin administration did not differ between experienced and non-experienced ICUs. Intravenous insulin administration was more likely to be initiated upon ICU admission (57% vs. 45%,  $p = 0.04$ ) and less likely after initial fluid resuscitation (27% vs. 35%,  $p = 0.04$ ) in experienced ICUs. Arterial or venous pH was monitored by 408(90%) respondents. Arterial blood gases were favored by 236(52%) respondents and venous blood gases were more likely to be performed in experienced ICUs (30% vs. 18%,  $p < 0.01$ ).

## Conclusions:

The management of patients with DKA remains heterogeneous worldwide. Future randomized trials are needed, especially regarding fluid resuscitation and insulin therapy.

# Background

Diabetic keto-acidosis (DKA) is the most common metabolic emergency in patients with diabetes, accounting for almost 10% of hospital admission in patients with diabetes [1]. There is currently an increase in hospital admissions for DKA [2, 3] and although the mortality rate for DKA remains low, ranging from 0.20% in patients with type 1 diabetes to 1.04% in those with type 2 diabetes, it has stopped decreasing over the last decade [2, 3].

DKA results from relative or absolute insulin deficiency and failure to regulate the effect of the hyperglycemic hormones glucagon, cortisol, growth hormone and catecholamines. The result is the hepatic metabolism of free fatty acids, which generates ketone bodies such as beta-hydroxybutyrate and acetoacetate [1, 4–6]. DKA is characterized by hyperglycemia leading to osmotic diuresis, which causes dehydration and water loss, and electrolyte imbalances (hypokalemia, hypophosphatemia, hypomagnesemia, and pseudohyponatremia), and metabolic acidosis linked to the production of ketone bodies [1, 3, 6]. The management of DKA requires fluid resuscitation, insulin therapy, and correction of metabolic disorders [3, 6–10]. The provision of continuous insulin therapy and the frequent monitoring and repletion of electrolytes requires critical care expertise and thus patients with DKA are admitted to the intensive care unit (ICU).

Guidelines for managing patients with DKA are limited [8–10]. While the American and British guidelines provide recommendations on fluid resuscitation and suggest isotonic saline as the first option [8, 10], the supporting evidence is limited, leading to ongoing debate regarding both fluid resuscitation, specifically regarding the use balanced solution to avoid the occurrence of hyperchloremic acidosis [3, 8–10]. Other heterogeneities in practice are related to insulin therapy, administration of sodium bicarbonate and the management of metabolic disorders.

This international survey aimed to assess current clinical management of adult patients with DKA, focusing on ICU admission criteria, fluid resuscitation, insulin therapy, and management of metabolic disorders.

## Methods

The survey was endorsed by the European Society of Intensive Care Medicine (ESICM) and was registered at the Institutional Review Board of Montpellier teaching Hospital (202,301,426) and used the snowball sampling method which allows respondents to forward the link to others using social medias and email lists. The survey included 39 items (Supplementary material) organized into three sections: [1] “Respondents, ICU characteristics and criteria for ICU admission”, [2] “Fluid resuscitation and insulin therapy” and [3] “Management of metabolic disorders and laboratory monitoring”.

## **Survey development**

The survey was introduced by a very short clinical snapshot to illustrate and contextualize it for all potential respondents. Survey questions were crafted in iterative fashion (by authors MJ and BJ) based on areas of uncertainty requiring more research from available international guidelines [9, 10]. First, all potential items of interest were independently identified from the current guidelines and listed by the two main authors of this survey (MJ and BJ). Then, all duplicate items were removed, and the remaining items were discussed between these two authors. Only the items with 100% concordance and agreement between the two authors were finally selected for the survey. Furthermore, the survey's items were double checked by a steering committee (EC and AL). Finally, the survey was pre and pilot tested in the two ICUs where the main authors (MJ and BJ) work and then adjusted according to the feedback that was obtained.

## **Survey Dissemination and population**

The survey was sent out electronically using SurveyMonkey Inc. ([www.surveymonkey.com](http://www.surveymonkey.com)). We opted for individual responses instead of a single ICU-wide response to account for potential practice variability among intensivists within the same unit. No personal data was collected, and participation did not require a login. To ensure completion and internal coherence, an alert prompted respondents before submitting the questionnaire, emphasizing mandatory unanswered questions. Post-submission review or modification of responses was not allowed. The survey was advertised on the ESICM website and open for participation from June to December 2023. All ESICM members were urged to join through an email containing a survey link sent to their email addresses in the ESICM membership database in June 2023, with two additional reminders in September and November 2023. In addition, the survey was publicized two times on the different ESICM's social networks. Participation was incentivized with a lottery for 10 respondents to win a sweatshirt from the University Cote d'Azur.

## **Survey reporting**

The methodology and findings of the survey are presented in accordance with the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) statement [11]. Ethical approval was deemed unnecessary given the voluntary nature of the survey and the absence of collection of individual patient data.

## **Statistical analysis**

Results were expressed as numbers (percentage) and were reported according to the experience of ICUs where the respondents practiced. Experienced ICUs were defined as ICU admitting over 20 patients with DKA per year. This threshold value was chosen (i) because it was the upper threshold value used in the survey to categorize the number of patients with DKA per year admitted to the ICUs where respondents are working and (ii), because this threshold value allowed us to describe approximately half of the respondents. We chose to compare the management of patients with DKA between experienced and non-experienced ICUs, because the experience of ICU most likely improves the homogeneity of management between physicians and the quality of patient care. We also compared the management of

patients with DKA depending on the income level of the countries according to the World Bank classification. Missing data were displayed with item denominators. Descriptive statistics were only carried out on the available data. Subgroup analyses were performed using chi-2 test or Fisher exact test as appropriate. All tests were two-sided and a  $p$  value  $< 0.05$  was considered statistically significant. All statistical analyses were performed using R (version 4.2.2, R foundation for Statistical Computing Vienna, Austria).

## Results

### Respondents

A total of 522 respondents from 57 different countries participated: 295(57%) worked in Europe, 86(16%) in North America, 25(5%) in South America, 52(10%) in Africa, 52(10%) in Asia and 12(2%) in Oceania (Fig. 1). Among them, 377(72%) worked in teaching hospitals, 147(28%) in medical ICUs, 355(68%) in medical-surgical ICUs, 20(4%) in surgical ICUs and 204(39%) in experienced ICUs). Respondents who worked in experienced ICUs were less likely to work in low or low-middle income countries (Table 1). The characteristics of respondents and ICUs according to the experience of ICU and the income level of the countries are summarized in Tables 1 and S1, respectively.

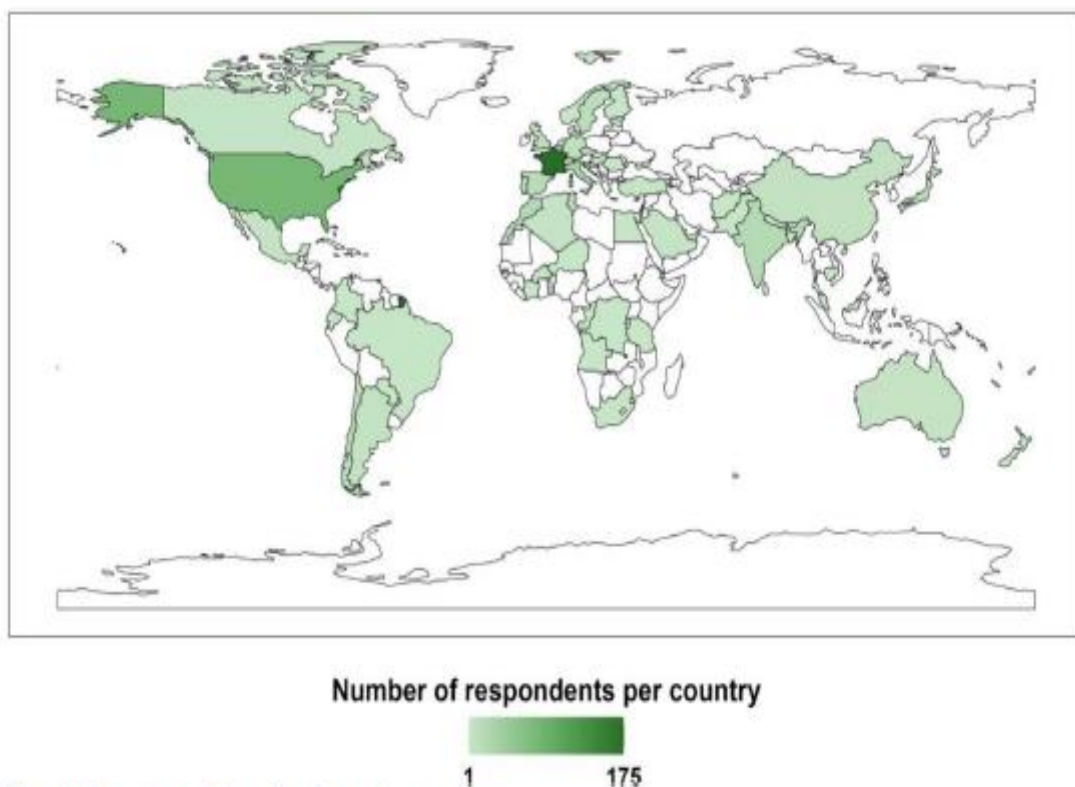


Fig. 1 World map showing the number of respondents per country

**Table 1** Respondent and ICU characteristics and criteria for ICU admission in experienced and non-experienced ICUs

|   | Respondents working in a non-experienced ICU<br><i>n</i> = 318 | Respondents working in an experienced ICU<br><i>n</i> = 204 | <i>p</i> value |
|---|--|---|----------------|
| Respondent and ICU characteristics ( <i>n</i> = 522)      |  |   |                |
| <i>World Bank country classifications by income level</i> |  |   |                |
| High Income   | 260 (82%)  | 158 (77%)   | 0.01           |
| Upper-Middle Income                                       | 24 (7%)  | 9 (4%)  |                |
| Lower-middle Income                                       | 29 (9%)  | 36 (18%)  |                |
| Low Income  | 5 (2%)   | 1 (1%)  |                |
| <i>Hospital characteristics</i>                           |  |   |                |
| Teaching hospital   | 216 (68%)  | 161 (79%)   | 0.02           |
| General hospital  | 91 (29%)   | 38 (19%)  |                |
| Other   | 11 (3%)  | 5 (2%)  |                |
| <i>ICU characteristics</i>                                |  |   |                |
| Medical ICU   | 70 (22%)   | 77 (38%)  | <0.001         |
| Surgical ICU  | 18 (6%)  | 2 (1%)  |                |
| Medical-Surgical ICU                                      | 230 (72%)  | 125 (61%)   |                |
| <i>Number of beds in ICU</i>                              |  |   |                |
| 8–12  | 121 (38%)  | 42 (21%)  | <0.001         |
| 12–20   | 105 (33%)  | 51 (25%)  |                |
| > 20  | 92 (29%)   | 111 (54%)   |                |
| <i>Nurse-to-patient ratio in ICU</i>                      |  |   |                |
| 1:1   | 34 (11%)   | 13 (6%)   | 0.46           |
| 1:2   | 114 (36%)  | 72 (35%)  |                |
| 1:3   | 44 (14%)   | 35 (17%)  |                |
| 1:4   | 12 (4%)  | 8 (4%)  |                |
| 1:2.5   | 110 (34%)  | 71 (35%)  |                |
| Other   | 4 (1%)   | 5 (3%)  |                |
| <i>Experience as Intensivist</i>                          |  |   |                |
| In training   | 39 (12%)   | 31 (15%)  | 0.68           |
| Full time < 2 years                                       | 34 (11%)   | 19 (9%)   |                |
| Full time between 2 and 5 years                           | 58 (18%)   | 32 (16%)  |                |
| Full time > 5 years                                       | 187 (59%)  | 122 (60%)   |                |
| <i>Criteria for ICU admission (<i>n</i> = 522)</i>        |  |   |                |
| <i>Arterial or venous pH value</i>                        |  |   |                |
| < 7.10  | 56 (18%)   | 28 (14%)  | 0.56           |
| < 7.20  | 84 (26%)   | 64 (31%)  |                |
| < 7.25  | 43 (14%)   | 24 (12%)  |                |
| < 7.30  | 36 (11%)   | 27 (13%)  |                |
| Not an admission criterion                                | 99 (31%)   | 61 (30%)  |                |
| <i>Arterial or venous bicarbonate concentration</i>       |  |   |                |
| < 5 mmol/L  | 12 (4%)  | 6 (3%)  | 0.43           |
| < 10 mmol/L   | 50 (16%)   | 29 (14%)  |                |
| < 15 mmol/L   | 65 (20%)   | 56 (28%)  |                |
| < 20 mmol/L   | 15 (5%)  | 7 (3%)  |                |
| Not an admission criterion                                | 176 (55%)  | 106 (52%)   |                |
| <i>Capillary or blood ketones</i>                         |  |   |                |
| > 2 mmol/L  | 21 (7%)  | 15 (7%)   | 0.92           |
| > 4 mmol/L  | 27 (8%)  | 16 (8%)   |                |
| > 6 mmol/L  | 21 (7%)  | 12 (6%)   |                |
| > 8 mmol/L  | 6 (2%)   | 2 (1%)  |                |
| Not an admission criterion                                | 243 (76%)  | 159 (78%)   |                |
| <i>Blood glucose</i>                                      |  |   |                |
| > 11 mmol/L   | 9 (3%)   | 4 (2%)  | 0.84           |
| > 15 mmol/L   | 19 (6%)  | 13 (6%)   |                |
| > 20 mmol/L   | 45 (14%)   | 25 (12%)  |                |
| Not an admission criterion                                | 245 (77%)  | 162 (80%)   |                |
| <i>Potassium concentration</i>                            |  |   |                |
| < 3 mmol/L  | 90 (28%)   | 50 (24%)  | 0.03           |
| < 3.2 mmol/L  | 22 (7%)  | 4 (2%)  |                |
| < 3.5 mmol/L  | 33 (10%)   | 28 (14%)  |                |
| Not an admission criterion                                | 173 (55%)  | 122 (60%)   |                |

**Table 1** (continued)

|  | Respondents working in a non-experienced ICU<br><i>n</i> = 318 | Respondents working in an experienced ICU<br><i>n</i> = 204 | <i>p</i> value |
|--|--|---|----------------|
| <i>Continuous intravenous insulin dose</i> |  |   | <0.01          |
| >5 UI/h                                    | 25 (7%)  | 16 (8%)   |                |
| 1–5 UI/h                                   | 28 (9%)  | 6 (3%)  |                |
| Any dose                                   | 101 (32%)  | 88 (43%)  |                |
| Not an admission criterion                 | 164 (52%)  | 94 (46%)  |                |

Data are summarized as number (percentage). ICU: intensive care unit

## Criteria for ICU admission

The pH value (< 7.20), arterial or venous bicarbonate concentration (< 15 mmol/L), and the need for continuous intravenous insulin (regardless of the dose) were considered criteria for ICU admission by 362(69%), 240(46%) and 264(51%) respondents, respectively. Capillary or blood ketones, blood glucose and serum potassium concentration were not considered as criteria for ICU admission for 402(77%), 407(78%) and 295(57%) respondents respectively. Serum potassium concentration was more likely to be considered as criteria for ICU admission in non-experienced ICUs, while intravenous insulin administration was more likely to be considered as criteria for ICU admission in experienced ICUs (Table 1, Fig. 2). Criteria for ICU admission according to the income level of the countries are summarized in Table S1.

## Fluid resuscitation

A protocol for initial fluid resuscitation was available for 290(63%) respondents and its availability did not differ between experienced and non-experienced ICUs (66% vs. 61%,  $p = 0.22$ ). Initial fluid resuscitation was based on physical examination, non-invasive hemodynamic monitoring and invasive monitoring in 292(63%), 161(35%) and 61(13%) of cases respectively (Table 2).

Overall, 135(29%) respondents administered isotonic saline only, 173(38%) administered balanced solutions only, and 153(33%) administered both. Fluid choice did not differ between experienced and non-experienced ICUs (Table 2, Fig. 3). Among balanced solutions, Ringer Lactate was used by 65% of respondents, Ringer acetate-gluconate (Plasmalyte®) by 11%, Ringer acetate-malate (Isosfundine®) by 14% and other balanced solutions by 10% of respondents. Sodium bicarbonate was administered by 166(36%) respondents and was more likely to be administered in non-experienced ICUs (43% vs. 25%,  $p < 0.001$ ) (Table 2, Fig. 3). The main indication of sodium bicarbonate administration was acidemia with pH < 7.10 (Table 2). The availability of a protocol influenced the management of initial fluid resuscitation, which was less often based on physical examination and non-invasive hemodynamic monitoring ( $p < 0.001$ ). It also influenced fluid choice, favoring more frequent use of isotonic saline only and less frequent administration of both saline and balanced solutions ( $p < 0.001$ ). Fluid resuscitation strategies according to the income level of the countries are summarized in Table S2.



## Insulin therapy

A protocol for insulin therapy was available for 355(77%) respondents and its availability did not differ between experienced and non-experienced ICUs (82% vs. 74%,  $p = 0.06$ ). An initial bolus of intravenous insulin was administered by 228(49%) respondents, 221(48%) used an initial continuous intravenous insulin dose of 0.1 UI/kg/h, 42(9%) used an initial predefined fixed dose, 159(35%) based the initial dose on blood glucose and 39(8%) on blood and/or urine ketones (Table 2). Overall, 436(95%) respondents administered intravenous glucose 5% concomitantly with intravenous insulin therapy, the most frequent threshold value being a blood glucose < 15 mmol/L. Modalities of intravenous insulin and glucose administration did not differ between experienced and non-experienced ICUs (Table 2 Fig. 4).

Intravenous insulin administration was initiated upon ICU admission by 230(50%) respondents, after initial fluid resuscitation by 147(32%) respondents and after potassium supplementation when potassium concentration was < 4.5 mmol/L by 84(18%) respondents. Intravenous insulin was more likely to be initiated upon ICU admission (57% vs. 45%,  $p = 0.04$ ) and less likely after initial fluid resuscitation (27% vs. 35%,  $p = 0.04$ ) in experienced ICUs (Table 2). The dose of continuous intravenous insulin was lowered as soon as capillary/blood or urine ketones disappeared by 243(53%) respondents, as soon as blood glucose was < 10 mmol/L by 159(35%) respondents, 12 h after the disappearance of capillary/blood or urine ketones by 45(10%) respondents and 24 h after the disappearance of capillary/blood or urine ketones by 14(2%) respondents (Table 2). Subcutaneous insulin was never resumed by 108(23%) respondents but was resumed more frequently and earlier in experienced ICUs (Table 2). The availability of a protocol influenced insulin therapy, with intravenous insulin more likely to be administered upon ICU admission ( $p = 0.02$ ), and subcutaneous insulin more likely to be resumed in ICU ( $p < 0.01$ ). Insulin therapy according to the income level of the countries is summarized in Table S2.

## Management of metabolic disorders

A protocol for potassium and phosphorus supplementation was available for 215(47%) respondents and was more likely to be available in experienced ICUs (55% vs. 41%,  $p < 0.01$ ). Potassium supplementation was more likely to be administered (90% vs. 79%,  $p = 0.001$ ) but less likely through a central venous catheter (31% vs. 44%,  $p < 0.01$ ) in experienced ICUs (Table 3). Threshold value for potassium supplementation did not differ between non- and experienced ICUs, and potassium supplementation was more likely to be administered when the potassium concentration was < 4 mmol/L (Table 3). All but three respondents considered renal replacement therapy to manage dyskalemia on the following criteria: dyskalemia-induced EKG abnormalities, associated dysnatremia and associated acute kidney injury. Management of metabolic disorders according to the income level of the countries is summarized in Table S3.

## Laboratory monitoring

Arterial or venous pH was monitored by 408(90%) respondents and arterial blood gases were favored by 236(52%) respondents. Venous blood gases were more likely to be performed in experienced ICUs (30% vs. 18%,  $p < 0.01$ ) and the pH value was more frequently monitored in non-experienced ICUs (Table 3). Arterial or venous bicarbonate concentration was monitored by 395(87%) respondents, with no difference between experienced and non-experienced ICUs (Table 3).

Capillary/blood or urine ketones were monitored by 282(62%) and 215(47%) respondents respectively. Urine ketones were more likely to be monitored in non-experienced ICUs (51% vs. 41%,  $p = 0.04$ ), while the frequency of capillary/blood or urine ketones did not differ between experiences and non-experienced ICUs (Table 3). Laboratory monitoring according to the income level of the countries is summarized in Table S3.

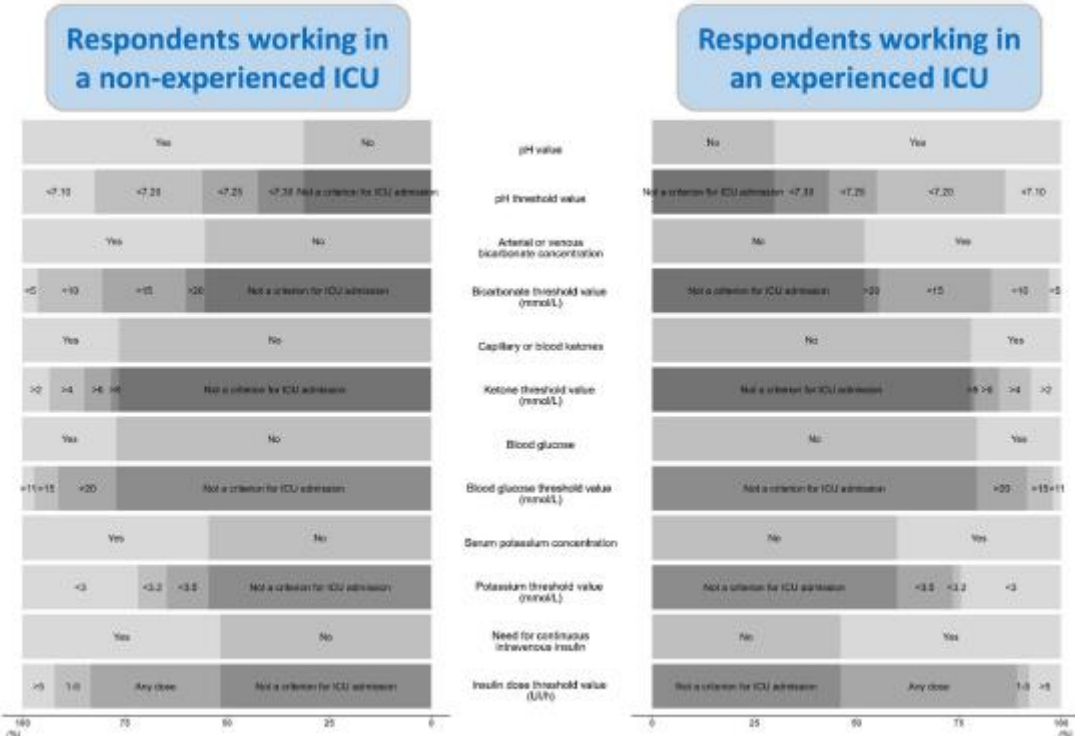


Fig. 2 Bar graphs showing the different criteria and their respective threshold values for admission to Intensive care unit (ICU) considered by respondents working in non-experienced (left panel) and in experienced (right panel) ICUs

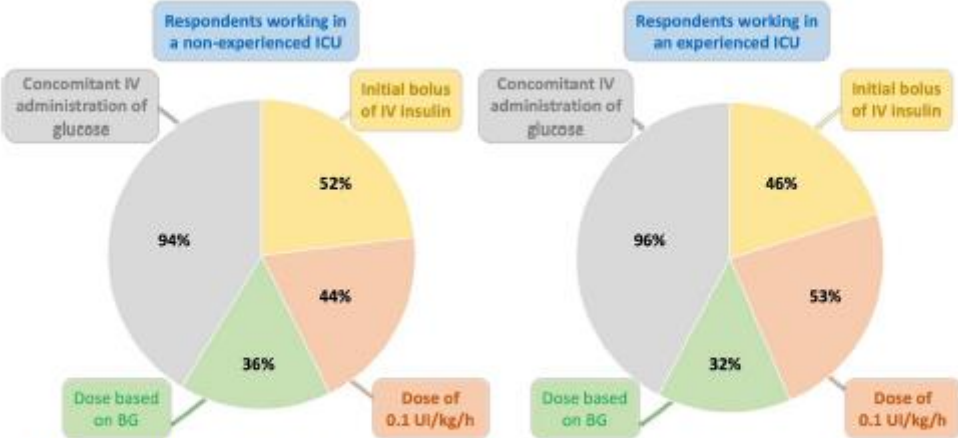


Fig. 4 Management of intravenous (IV) insulin therapy by respondents working in a non-experienced and in experienced intensive care unit (ICU). Each pie-chart indicates the proportion of respondents who report performing an initial bolus of IV insulin, using a continuous IV insulin dose of 0.1 U/kg/h, basing the dose of continuous IV insulin on blood glucose (BG) and administering IV glucose concomitantly with IV insulin therapy

## Discussion

The current level of evidence on the management of adult patients with DKA is scarce. This survey highlights significant heterogeneity regarding the management of these patients, based on the experience of ICU and the income level of the countries according to the World

**Table 2** Fluid resuscitation and Insulin therapy In experienced and non-experienced ICUs

|   | Respondents working<br>in a non-experienced<br>ICU<br>n= 318 | Respondents working<br>in an experienced ICU<br>n= 204 | p value |
|---|--|--|---------|
| Fluid resuscitation (n= 461)  |  |  |         |
| Protocol available  | 168 (61%)  | 122 (60%)  | 0.22    |
| Initial fluid resuscitation based on physical examination                               | 191 (69%)  | 101 (55%)  | <0.001  |
| Initial fluid resuscitation based on non-invasive hemodynamic monitoring                | 102 (37%)  | 59 (32%)   | 0.29    |
| Initial fluid resuscitation based on invasive hemodynamic monitoring                    | 43 (16%)   | 18 (10%)   | 0.08    |
| Fluids administered   |  |  | 0.23    |
| Isotonic saline only  | 73 (26%)   | 62 (34%)   |         |
| Balanced solutions only   | 107 (39%)  | 66 (36%)   |         |
| Both types of fluids  | 97 (35%)   | 56 (30%)   |         |
| Intravenous sodium bicarbonate administration   | 120 (43%)  | 46 (25%)   | <0.001  |
| Type of sodium bicarbonate  |  |  | 0.25    |
| 1.4% only   | 34 (28%)   | 18 (39%)   |         |
| 4.2% only   | 27 (22%)   | 12 (26%)   |         |
| 8.4% only   | 54 (45%)   | 13 (28%)   |         |
| Use of different types  | 5 (4%)   | 3 (7%)   |         |
| Sodium bicarbonate administration based on pH value                                     | 107 (89%)  | 44 (96%)   | 0.24    |
| pH value considered for sodium bicarbonate administration                               |  |  | 0.04    |
| < 6.90  | 20 (19%)   | 16 (36%)   |         |
| < 7.00  | 28 (26%)   | 12 (27%)   |         |
| < 7.10  | 59 (55%)   | 16 (37%)   |         |
| Sodium bicarbonate administration based on arterial or venous bicarbonate concentration | 86 (72%)   | 29 (63%)   | 0.37    |
| Bicarbonate concentration considered for sodium bicarbonate administration              |  |  | 0.09    |
| < 10 mmol/L   | 66 (77%)   | 17 (59%)   |         |
| < 5 mmol/L  | 20 (23%)   | 12 (41%)   |         |
| Sodium bicarbonate administration based on potassium concentration                      | 50 (42%)   | 22 (48%)   | 0.59    |
| Potassium concentration considered for sodium bicarbonate administration                |  |  | 0.79    |
| > 6 mmol/L  | 31 (62%)   | 15 (68%)   |         |
| > 6.5 mmol/L  | 19 (38%)   | 7 (32%)  |         |
| Other indications for sodium bicarbonate administration                                 | 10 (8%)  | 0 (0%)   | 0.06    |
| Insulin therapy (n= 461)  |  |  |         |
| Protocol available  | 205 (74%)  | 150 (82%)  | 0.06    |
| Administration of an initial bolus of intravenous insulin                               | 144 (52%)  | 84 (46%)   | 0.18    |
| Initial continuous intravenous insulin dose   |  |  | 0.62    |
| 0.1 U/Kg/h  | 123 (44%)  | 98 (53%)   |         |
| Fixed dose of 5 U/h   | 9 (3%)   | 5 (3%)   |         |
| Fixed dose of 8 U/h   | 4 (2%)   | 2 (1%)   |         |
| Fixed dose of 10 U/h  | 14 (5%)  | 8 (4%)   |         |
| Dose based on blood glucose   | 101 (36%)  | 58 (32%)   |         |
| Dose based on blood and/or urine ketones  | 26 (10%)   | 13 (7%)  |         |
| Timing of intravenous insulin initiation  |  |  | 0.04    |
| Upon ICU admission  | 125 (45%)  | 105 (57%)  |         |
| After initial fluid resuscitation   | 98 (35%)   | 49 (27%)   |         |
| After potassium supplementation when potassium concentration < 4.5 mmol/L               | 54 (20%)   | 30 (16%)   |         |
| Timing of continuous intravenous insulin dose lowering                                  |  |  | 0.59    |
| As soon as capillary or blood ketones disappeared                                       | 101 (36%)  | 79 (43%)   |         |
| As soon as urine ketones disappeared  | 40 (15%)   | 23 (13%)   |         |
| 12 h after the disappearance of capillary or blood ketones                              | 21 (8%)  | 17 (9%)  |         |

**Table 2** (continued)

|   | Respondents working<br>in a non-experienced<br>ICU<br><i>n</i> = 318 | Respondents working<br>in an experienced ICU<br><i>n</i> = 204 | <i>p</i> value |
|---|--|--|----------------|
| 12 h after the disappearance of urine ketones                                     | 5 (2%)   | 2 (1%)   |                |
| 24 h after the disappearance of capillary or blood ketones                        | 3 (1%)   | 4 (2%)   |                |
| 24 h after the disappearance of urine ketones                                     | 4 (1%)   | 3 (2%)   |                |
| As soon as blood glucose < 10 mmol/L  | 103 (37%)  | 56 (30%)   |                |
| Timing of subcutaneous insulin resumption   |  |  | <0.001         |
| Never in ICU  | 81 (29%)   | 27 (15%)   |                |
| Upon ICU admission in addition to intravenous insulin                             | 25 (9%)  | 37 (20%)   |                |
| After a certain period of continuous intravenous insulin                          | 171 (62%)  | 120 (65%)  |                |
| Intravenous glucose administration concomitantly with intravenous insulin therapy | 259 (94%)  | 177 (96%)  | 0.21           |
| Type of glucose solution ( <i>n</i> = 346*)                                       |  |  | 0.98           |
| Glucose 5% only   | 108 (52%)  | 70 (51%)   |                |
| Glucose 10% only  | 57 (27%)   | 36 (26%)   |                |
| Glucose 30% only  | 3 (1%)   | 2 (2%)   |                |
| Use of different types  | 41 (20%)   | 29 (21%)   |                |
| Threshold value for glucose administration ( <i>n</i> = 242*)                     |  |  | 0.76           |
| As soon as blood glucose < 15 mmol/L  | 70 (51%)   | 52 (50%)   |                |
| As soon as blood glucose < 10 mmol/L  | 54 (39%)   | 44 (42%)   |                |
| As soon as blood glucose < 8 mmol/L   | 14 (10%)   | 8 (8%)   |                |

Data are summarized as number (percentage). ICU: intensive care unit

\* Among the 436 respondents who administer glucose concomitantly with insulin therapy

### Bank classification.

We found significant heterogeneity in fluids administered to patients with DKA. Although evidence does not support routine systemic alkalization, one-third of respondents reported using sodium bicarbonate, typically for pH < 7.10. DKA-related acidosis does not impair cardiac contractility [12], and sodium bicarbonate may delay hyperglycemia and DKA recovery [13–15] while increasing the risk of cerebral edema, especially in children [4, 16]. Guidelines limits its use in patients with pH < 7.0 [9, 10].

The choice between isotonic and balanced solutions remains debated in the critical care community [17–22], including in patients with DKA [23–26]. Two small randomized controlled trials (< 60 patients, one of which was stopped prematurely) evaluating the use of balanced solutions in patients with DKA found contradictory results, both in terms of recovery speed of DKA and the incidence of fluid-related metabolic disorders [23, 24]. Secondary analyses of two pragmatic trials (SALTED and SMART trials) showed that balanced solutions (Plasma-Lyte-A or Ringer Lactate) were associated with faster DKA recovery and a shorter duration of intravenous insulin administration [25]. The SCOPE-DKA trial, which compared a balanced solution (Plasmalyte-148) with isotonic saline in 93 patients admitted to ICU for DKA, found no difference in the primary outcome, which was the increase in base excess > -3 mEq/L at 48 h of management [26]. Importantly, in these trials, crossover rates between randomization arms ranged from 30 to 50% [25, 26], and none of these studies had a dedicated protocol for fluid administration [24–26]. A recent metaanalysis encompassing these randomized trials found that balanced solutions compared to isotonic saline might accelerate DKA resolution and reduce the frequency of hyperchloremic metabolic acidosis. Still, the amount of fluid administered, and the duration of intravenous insulin administration did not differ between groups [27]. Recent consensus reports from American, British and European diabetes societies now suggests the use of either isotonic saline or balanced solutions, depending on local availability, cost and resources [1, 3, 6]. Nonetheless, further randomized trials, like the ongoing DRINK trial (NCT 06541535), are needed to further clarify the optimal fluid choice.

**Table 3** Management of metabolic disorders and laboratory monitoring in experienced and non-experienced ICUs

|   | Respondents working in a non-experienced ICU<br>n=318 | Respondents working in an experienced ICU<br>n=204 | p value |
|---|---|--|---------|
| <b>Management of metabolic disorders (n=522)</b>  |   |  |         |
| <i>Potassium and phosphorus supplementation protocol</i>  | 155 (49%)   | 121 (59%)  | 0.02    |
| <i>Potassium administration through a central venous catheter</i>   | 121 (38%)   | 58 (28%)   | 0.03    |
| <i>Threshold value for potassium administration (n=384*)</i>  |   |  |         |
| <i>As soon as potassium concentration &lt; 5.5 mmol/L</i>   | 30 (13%)  | 24 (14%)   | 0.40    |
| <i>As soon as potassium concentration &lt; 5.0 mmol/L</i>   | 47 (22%)  | 28 (17%)   |         |
| <i>As soon as potassium concentration &lt; 4.5 mmol/L</i>   | 49 (22%)  | 51 (31%)   |         |
| <i>As soon as potassium concentration &lt; 4.0 mmol/L</i>   | 91 (42%)  | 62 (37%)   |         |
| <i>Systematic potassium administration as soon as &gt;2 h after the introduction of intravenous insulin</i> | 1 (1%)  | 1 (1%)   |         |
| <b>Laboratory monitoring (n=453)</b>  |   |  |         |
| <i>Capillary or blood ketones monitoring</i>  | 171 (63%)   | 111 (61%)  | 0.82    |
| <i>Frequency of capillary or blood ketones monitoring in the first 24 h of management</i>                   |   |  |         |
| <i>Hourly</i>   | 37 (22%)  | 25 (23%)   | 0.46    |
| <i>Per 2 h</i>  | 44 (25%)  | 33 (30%)   |         |
| <i>Per 4 h</i>  | 36 (21%)  | 19 (17%)   |         |
| <i>Per 6 h</i>  | 20 (12%)  | 7 (6%)   |         |
| <i>Other</i>  | 34 (20%)  | 27 (24%)   |         |
| <i>Urine ketones monitoring</i>   | 140 (51%)   | 75 (41%)   | 0.04    |
| <i>Frequency of urine ketones monitoring in the first 24 h of management</i>                                |   |  |         |
| <i>Hourly</i>   | 15 (10%)  | 10 (13%)   | 0.66    |
| <i>Per 2 h</i>  | 13 (9%)   | 10 (13%)   |         |
| <i>Per 4 h</i>  | 25 (18%)  | 12 (16%)   |         |
| <i>Per 6 h</i>  | 40 (29%)  | 24 (32%)   |         |
| <i>Other</i>  | 47 (34%)  | 19 (26%)   |         |
| <i>Arterial or venous pH monitoring</i>   | 250 (92%)   | 158 (87%)  | 0.15    |
| <i>Type of blood gases</i>  |   |  |         |
| <i>Arterial blood gases only</i>  | 157 (63%)   | 79 (50%)   | 0.01    |
| <i>Venous blood gases only</i>  | 45 (18%)  | 48 (30%)   |         |
| <i>Arterial or venous blood gases</i>   | 48 (19%)  | 31 (20%)   |         |
| <i>Frequency of arterial or venous pH monitoring in the first 24 h of management</i>                        |   |  |         |
| <i>Hourly</i>   | 27 (11%)  | 6 (4%)   | <0.01   |
| <i>Per 2 h</i>  | 51 (20%)  | 23 (15%)   |         |
| <i>Per 4 h</i>  | 74 (30%)  | 45 (28%)   |         |
| <i>Per 6 h</i>  | 68 (27%)  | 51 (32%)   |         |
| <i>Other</i>  | 30 (12%)  | 33 (21%)   |         |
| <i>Arterial or venous bicarbonate concentration monitoring</i>  | 242 (89%)   | 153 (85%)  | 0.21    |
| <i>Frequency of arterial or venous bicarbonate concentration monitoring in the first 24 h of management</i> |   |  |         |
| <i>Hourly</i>   | 22 (9%)   | 5 (3%)   | 0.11    |
| <i>Per 2 h</i>  | 44 (18%)  | 21 (14%)   |         |
| <i>Per 4 h</i>  | 78 (32%)  | 51 (33%)   |         |
| <i>Per 6 h</i>  | 67 (28%)  | 52 (34%)   |         |
| <i>Other</i>  | 31 (13%)  | 24 (16%)   |         |

Data are summarized as number (percentage). ICU: intensive care unit

\* Only 384 respondents administered potassium supplementation

This survey also found a significant heterogeneity in the timing of intravenous insulin initiation, the use of an initial bolus, initial doses and dose adjustment criteria for continuous intravenous insulin. Half of the respondents started intravenous insulin prior to or simultaneously with fluid resuscitation as recommended [3, 10]. Interestingly, experienced ICUs were less likely to start intravenous insulin after initial fluid resuscitation. Our results align with previous French and Canadian surveys [7, 28]. In the French survey, intravenous insulin therapy was started prior to fluid resuscitation by 7% of respondents, simultaneously by 46%, and after fluid resuscitation by 47%. The rationale for delaying insulin until after fluid resuscitation was likely to reduce the risk of hypokalemia associated with dehydration [7]. In the Canadian survey, intravenous insulin therapy was typically started 25 min after fluid resuscitation began [28].

The use of an initial intravenous bolus of insulin varied significantly, with 49% of respondents administering one, a higher rate than in previous French (27%) and Canadian (43%) surveys [7, 28]. Current guidelines recommend against an initial bolus of insulin [3, 9, 10], unless there is a delay in starting continuous intravenous insulin [3, 10], but clinical practice may be influenced by findings of a small randomized trial suggesting that low-dose continuous intravenous insulin ( $< 0.1$  UI/kg/h) without an initial bolus may result in an insufficient insulin concentration to suppress hepatic production of ketones [29]. Furthermore, 48% of respondents adhered to the recommended initial continuous intravenous insulin dose of 0.1 UI/ kg/h [3, 9, 10]. This recommended dose is higher than that reported in the French and Canadian surveys [7, 28]. Additionally, the French survey reported that patients with type 1 or newly diagnosed diabetes received lower continuous intravenous insulin doses than patients with type 2 or secondary diabetes, suggesting an increased insulin resistance in these patients [7].

More than half of respondents reported lowering the continuous intravenous insulin dose after the disappearance of ketones, while 35% did so when blood glucose dropped below a defined threshold, as recommended [3, 8, 10]. Although ketones monitoring is recommended in patients with DKA [3, 8, 10], relying solely on urine ketones may delay the assessment of treatment efficacy, as it only detects acetoacetate but not  $\beta$ -hydroxybutyrate, which is oxidized to acetoacetate and eliminated in the urine [30]. Whatever the timing for lowering the continuous intravenous insulin dose, it is crucial to administer continuous intravenous insulin until DKA resolution to block lipolysis and prevent further ketones generation [3, 8, 10]. The timing of the transition from intravenous to subcutaneous insulin was also heterogeneous and 23% of respondents never resumed subcutaneous insulin in ICU. Nevertheless, adding subcutaneous basal insulin to continuous intravenous insulin may hasten DKA resolution, shorten the duration of intravenous insulin administration, and prevent rebound hyperglycemia without increasing the risk of hypoglycemia or other metabolic disorders [3, 8, 10].

Finally, 90% of respondents preferred analyzing arterial over venous blood gas samples, even though the advantage of arterial sampling has yet to be proven [31]. In addition, the insertion of an arterial catheter is painful, associated with vascular, thrombotic and infectious complications [32, 33] and may lead to more frequent and unnecessary samples increasing the risk of anemia and costs [34].

The main strength of this worldwide, large, survey is to provide a comprehensive snapshot of current management of patients with DKA and to highlight the existing heterogeneity in their management. It focuses on the main aspects of DKA management, from ICU admission criteria to fluid resuscitation, insulin therapy, and the management of metabolic disorders.

There are some significant limitations to the survey. First, as we used emails and social networks, we could not calculate the response rate as we had no access to the denominator. Second, the external validity of our findings could be limited, as certain centers may have been overrepresented, and our findings only reflected the opinion of intensivists who chose to participate in the survey. Therefore, the results of this survey, like those of all surveys, must be interpreted with caution due to the nature of data capture. Third, we did not collect further data on the available protocols for fluid resuscitation and insulin therapy, including the existence of hospital or emergency department protocols for DKA management outside the ICU. It was therefore not possible to assess whether protocols differed from one another or whether respondents did not follow them to explain the heterogeneity we found. Nevertheless,

this international survey highlights the existing heterogeneity in the management of patients with DKA worldwide and may indicate future directions for research. Fourth, as the number of questions in the survey was limited in an attempt to obtain a satisfactory response rate, many criteria for ICU admission (such as shock, organ failure, site policies etc....) were not evaluated. Nevertheless, we focused on the clinical and biological criteria reported in the current guidelines [3, 8–10]. Finally, the type of underlying diabetes (type 1 diabetes, type 2 diabetes or secondary diabetes) was not collected, even though there are pathophysiological differences that could influence DKA management [7]. Nevertheless, current guidelines do not distinguish between these patients [3, 8–10] and the resolution time of DKA did not differ according to the type of diabetes [7].

## Conclusions

The management of adult patients with DKA remains heterogeneous worldwide. Further randomized trials on the management of these patients are needed, especially regarding fluid resuscitation and insulin therapy.

### Abbreviations

DKA Diabetic keto-acidosis  
ICU Intensive care unit

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### Author contributions

MJ and BJ conceived and designed the survey. MJ, MH, EC, AL, MMD, NM and BJ analyzed and interpreted the data. MJ and BJ drafted the first version of the manuscript report. All authors contributed drafting the manuscript and approved the final version of the manuscript.

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### Availability of data and materials

No datasets were generated or analysed during the current study.

## **Declarations**

### **Ethics approval and consent to participate**

The survey was endorsed by the European Society of Intensive Care Medicine (ESICM) and was registered at the Institutional Review Board of Montpellier teaching Hospital (202301426).

### **Consent for publication**

Not applicable.

### **Competing interests**

The authors declare no competing interests.

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