



Research paper

Opinions and practices of blood glucose control in critically ill patients with pre-existing type 2 diabetes in Australian and New Zealand intensive care units[☆]



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Background: Approximately 9000 patients with type-2 diabetes mellitus (T2DM) are admitted to an intensive care unit (ICU) in Australia and New Zealand annually. For these patients, recent exploratory data suggest that targeting a more liberal blood glucose range during ICU admission may be safe and potentially beneficial. However, the current approach to blood glucose management of patients with T2DM in Australia and New Zealand ICUs is not well described, and there is uncertainty about clinician equipoise for trials of liberal glycaemic control in these patients.

Aim: The aim is to describe self-reported blood glucose management in patients with T2DM by intensivists working in Australian and New Zealand ICUs and to establish whether equipoise exists for a trial of liberal versus standard glycaemic control in such patients.

Method: An online questionnaire of Australia and New Zealand intensivists conducted in July–September 2016.

Results: Seventy-one intensivists responded. Forty-five (63%) used a basic nomogram to titrate insulin. Sixty-six (93%) reported that insulin was commenced at blood glucose concentrations >10 mmol/L and titrated to achieve a blood glucose concentration between 6.0 and 10.0 mmol/L. A majority of respondents (75%) indicated that there was insufficient evidence to define optimal blood glucose targets in patients with T2DM, and 59 (83%) were prepared to enrol such patients in a clinical trial to evaluate a more liberal approach.

Conclusion: A majority of respondents were uncertain about the optimal blood glucose target range for patients with T2DM and would enrol such patients in a comparative trial of conventional versus liberal blood glucose control.

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1. Introduction

Patients with type-2 diabetes mellitus (T2DM) are frequently admitted to an intensive care unit (ICU).^{1,2} Hyperglycaemia, defined as >10 mmol/L, occurs frequently in this group, and management of hyperglycaemia in ICU is nearly always protocolised.^{3–5} Such protocols promote uniformity of practice and improve the overall quality of care; however, if applied uniformly across all patient subgroups, as a consequence of inadequate data, may lead to harm.⁶

The current approach to blood glucose management is to implement the same protocol for those with and without diabetes, typically to target a range of 6–10 mmol/L. Such practice has largely been informed by the findings of the Normoglycaemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial.⁷ More recent observational and exploratory data suggest that, for patients with diabetes, titrating intravenous insulin to target blood glucose concentrations between 10 and 14 mmol/L during ICU admission may be safe and potentially beneficial.^{1,8–13} Moreover, the excessive administration of insulin may itself lead to a disturbance in the ability of the body to regulate glucose concentration effectively and may be associated with increased mortality.⁷ Because of these effects, and the potential impact on survival, allowing a 'liberal' approach to glucose control (a tolerance of higher blood glucose concentrations than are targeted in patients with previously normal glucose tolerance) may be beneficial for patients with T2DM.^{1,8–15} Before any large randomised controlled trial to evaluate a more liberal approach in this cohort, it is important to have an understanding of Australian and New Zealand practice and clinician concerns and preferences toward such a liberal approach.

In response, we surveyed intensivists in Australian and New Zealand to study their attitudes, preferences, and self-reported practice of glucose management for patients with T2DM admitted to ICU. In particular, we wanted to identify how intensivists monitor and respond to blood glucose concentrations and their level of concern about a liberal glucose management approach. Finally, we enquired whether intensivists would be

willing to enrol patients with T2DM in a randomised trial comparing the safety and efficacy of liberal versus conventional glycaemic management in the ICU.

2. Methods

2.1. Survey

We used an anonymous, structured, multichoice online questionnaire to survey intensivists (<https://www.surveymonkey.com/r/55G785D>). The questionnaire consisted of twenty-two questions divided into four parts: (1) the basic demographic details of respondents, (2) current approach to blood glucose monitoring, (3) current management of glycaemia, and (4) opinions on the current evidence for management of glycaemia in critically ill patients with T2DM. This survey was approved by the Royal Adelaide Hospital Human Research Ethics Committee.

2.2. Target population and questionnaire administration

Australian and New Zealand intensivists were identified using the Australian and New Zealand Intensive Care Society (ANZICS) and the ANZICS Clinical Trials Group (ANZICS-CTG) databases. This target population included paediatric and adult intensivists. Each intensivist was invited by email to respond to the online questionnaire. Eight weeks after the initial email invitation, a single reminder email was sent. All responses were recorded during an 11-week period, from 12/07/2016 to 29/09/2016.

2.3. Data management and analysis

Response data were downloaded from SurveyMonkey™ directly into an Excel spreadsheet (XLS, Microsoft Excel®). Responses are shown as number (%) for each given question, with 95% exact binomial confidence intervals (CIs). Data were analysed using descriptive statistical procedures to calculate means and percentages. No imputation was undertaken for missing data. All quantitative analyses were performed using Excel 2010 (Microsoft®).

3. Results

3.1. Cohort characteristics and glucose monitoring

The survey invitation email was sent to 1605 ANZICS and ANZICS-CTG subscribers, with 71 (4%) responding to the survey with their cumulative responses recorded in Table 1. The majority 49/70 (70%, CI: 57.9–80.4) were primarily employed in public metropolitan hospitals, 14/70 (20%, CI: 11.4–31.3) practices in New Zealand ICUs, 56/70 (80%, CI: 68.7–88.6) from Australian ICUs with Victoria, New South Wales, and the North Island of New Zealand representing 44/70 (63%) of respondents, and 37/70 (53%) of respondents had more the 10 years of ICU specialist experience (Supplemental Table 1). Excluding protocols for patients with diabetic ketoacidosis,¹⁶ 38/70 (54%, CI: 41.3–65.5) reported that their ICU had no specific protocol for patients with T2DM. Glucometers 36/71 (51%, CI: 38.6–62.8) and arterial blood gas analysers 35/71 (49%, CI: 37.2–61.4) were equally reported as the predominant method used to monitor blood glucose concentrations.

3.2. Management of blood glucose concentrations

Forty-five of 71 (63%, CI: 51.1–74.5) respondents reported using a basic nomogram to titrate therapy with intravenous insulin (Table 2). Sixty-six of 71 (93%, CI: 84.3–97.7) respondents replied that insulin is commenced with a blood glucose concentration above 10 mmol/L and titrated to achieve blood glucose concentrations between 6 and 10 mmol/L (Table 2).

3.3. Type 2 diabetes

With regard to patients with pre-existing diabetes, 4/70 (6%, CI: 1.6–14.0) respondents had major concerns, and 48/70 (68%, CI: 56.4–79.1) did not have major concern with causing harm by not treating blood glucose concentrations at a threshold of 10 mmol/L; 27/71 (38%, CI: 26.8–50.3) strongly agreed, and 28/71 (39%, CI: 28.0–51.7) agreed that the results of NICE-SUGAR have influenced the approach to glycaemia in ICU (Table 2). There is currently sufficient evidence to determine the optimal blood glucose range for patients with T2DM admitted to the ICU; 15/70 (21%, CI: 12.5–32.9)

Table 1
Monitoring and management of blood glucose concentrations for patients with type 2 diabetes admitted to ICU.

Clinical scenarios and response options	Responses n (% ^a)	CI
Predominant method to measure blood glucose (71 ^b)		
Point of care glucometer	36 (51%)	38.6, 62.8
Arterial blood gas machine	35 (49%)	37.2, 61.4
Central laboratory	0 (0%)	0.0, 5.1
Excluding protocols for patients admitting for diabetic ketoacidosis, does your ICU have a blood glucose management protocol that is specific to patients with diabetes? (70 ^b)		
No	38 (54%)	41.3, 65.5
Yes	28 (40%)	28.0, 51.7
Unsure	4 (6%)	1.6, 13.8
How frequently (on average) do you think that blood glucose concentrations are measured in your ICU from patients with diabetes with an arterial line in situ? (71 ^b)		
At least 4 hourly	36 (51%)	38.6, 62.8
At least 6 hourly	26 (37%)	25.5, 48.9
At least 2 hourly	7 (10%)	4.1, 19.3
Hourly	1 (1%)	0.0, 7.6
Daily	1 (1%)	0.0, 7.6
Continuously	0 (0%)	0.0, 5.1
Never	0 (0%)	0.0, 5.1

ICU, intensive care unit; CI, confidence interval.

^a Percentage of the total number of responses for that question.

^b Number of responses.

agreed, 16/70 (23%, CI: 13.7–34.4) neutral, 26/70 (37%, CI: 25.9–49.5) disagreed, and 11/70 (16%, CI: 8.1–26.4) strongly disagreed (Table 2). Four of 71 (6%, CI: 1.6–13.8) strongly agreed, and 20/71 (41%, CI: 29.3–53.2) agreed that they were concerned about an increased risk of infection with liberal glycaemic control (Table 2). Thirty-three of 71 (46%, CI: 34.5–58.7) were concerned about the potential risk of hypoglycaemia (<4.0 mmol/L) when aiming for blood glucose concentrations between 6 and 10 mmol/L in patients with T2DM, with 35% of respondents were not concerned (Table 2). Forty-one of 71 (58%, CI: 45.4–69.4) respondents considered that blood glucose concentration range between 6 and 10 mmol/L was safe for T2DM (Table 2). Seventeen of 71 (24%, CI: 14.6–35.5) strongly agreed, and 28/71 (39%, CI: 28.0–51.7) agreed that they were willing to enrol T2DM patients in a trial of liberal glycaemic control, regardless of the admission diagnostic category, but fewer physicians were willing to enrol postoperative than medical patients with T2DM (Table 2). Forty-four of 71 (63%, CI: 49.7–73.2) participants think that it is feasible to have two glucose protocols—one for patients with diabetes and one for patients without diabetes.

4. Discussion

The intensive care specialists who responded from Australia and New Zealand suggest that the most frequently targeted blood glucose range for patients with T2DM is 6–10 mmol/L, with less than half of intensivists responding and reporting a specific protocol for patients with T2DM. There was no consensus as to whether there was sufficient evidence to guide management in critically ill patients with T2DM, and only a minority would be unwilling to evaluate a more liberal strategy in this group of patients.

4.1. Strengths and weakness

Our study provides some insights into the management and concerns with glucose control in T2DM patients as reported by surveyed ANZ intensivists. The respondents came from a mixture of adult ICUs and spread across most states, territories, and New Zealand. There are, however, significant limitations. Invitations were sent using the ANZICS and ANZICS-CTG databases and may not be fully representative of the broader community of ICU specialists. Responses were self-reported and so may not reflect actual practice. Electronic surveys conducted via email invitations traditionally have low response rates,¹⁷ as was the case with this survey, and such responses may not reflect wider population opinions.^{17,18} However, the response rate for our survey was consistent with others using this method¹⁸ and reflect the uncertainty within the literature.^{9,19}

4.2. Implications

Recent literature reviews have focused on glycaemic control in critically ill patients with T2DM, particularly regarding the potential for harm from hypoglycaemia and the rationale for a different approach than that used for critically ill patients without diabetes.²⁰ Such observations are supported by recent exploratory studies.^{8,9,12,14} The recent observational data have suggested that blood glucose concentrations that are frequently associated with harm in patients with 'normal' glucose tolerance may be less desirable in patients with T2DM.^{1,4,6,8,14} The majority of responses provided replies that were consistent with the uncertainty. No studies have specifically explored the current practice of blood glucose management of critically ill patients with T2DM in Australian and New Zealand ICUs, and while limited in scope, this study provides some insights into the current practice of the respondents. Based on this uncertainty, a phase II trial has been planned to further evaluate this issue (ACTRN number 12616001135404).

Table 2

Current practice and current evidence for glucose control in patients with type 2 diabetes admitted to ICU.

Clinical scenarios and response options	Responses n (%) ^a	CI
Of the following options, please indicate what algorithm you predominantly use when treating hyperglycaemia in patients within your ICU. (71 ^{b,c})		
Basic nomogram	45 (63%)	51.1, 74.5
Dynamic protocol	13 (18%)	10.1, 29.3
Dynamic protocol that incorporates nutritional intake as well	2 (3%)	0.3, 9.8
Computerised protocols	3 (4%)	0.9, 11.9
No protocol used	8 (11%)	5.0, 21.0
Which of the following methods would you initially use when treating hyperglycaemia in T2DM patients expected to stay longer than 24 h in ICU: (71 ^{b,c})		
Subcutaneous insulin administration only	3 (4%)	0.9, 11.9
Subcutaneous insulin followed by intravenous insulin administration	3 (4%)	0.9, 11.9
Intravenous insulin therapy only	39 (55%)	42.7, 66.8
Intravenous insulin therapy followed by subcutaneous insulin	23 (32%)	21.8, 44.5
I do not mind which mode of therapy is initially used, so I let the junior medical staff decide	3 (4%)	0.9, 11.9
In the unit that you predominantly work and according to that protocol when insulin commenced in ICU patients. (71 ^b)		
Insulin is started for blood glucose \geq 6.1 mmol/L and titrated to achieve blood glucose concentrations 4.5–6.0 mmol/L as per Leuven studies	0 (0%)	0.0, 5.1
Insulin is started for blood glucose \geq 10.1 mmol/L and titrated to achieve blood glucose concentrations between 6.0 and 10.0 mmol/L as per the NICE-SUGAR	66 (93%)	84.3, 97.7
Neither, as insulin is started at a threshold blood glucose concentration greater than Leuven but less than the NICE-SUGAR (i.e. between 6.1 and 10.0 mmol/L)	2 (3%)	0.3, 9.8
Neither, as insulin is started at a threshold greater than the NICE-SUGAR.	3 (4%)	0.9, 11.9
In patients with diabetes, when would you commence treatment for a blood glucose level of $>$ 14 mmol/L? (71 ^b)		
<1 Hour	42 (59%)	46.8, 70.7
1–2 Hours	23 (32%)	21.8, 44.5
2–4 Hours	4 (6%)	1.6, 13.8
4–6 Hours	2 (3%)	0.3, 9.8
>6 Hours	0 (0%)	0.0, 5.1
Never	0 (0%)	0.0, 5.1
Please indicate how concerned you are about inducing further harm associated with not treating blood glucose concentrations $>$ 10 mmol/L in patients without pre-existing diabetes? (70 ^{b,c})		
Yes, this is a major concern	11 (15%)	8.0, 26.0
Yes, but not a major concern	49 (69%)	56.9, 79.5
No, it is not a concern	11 (15%)	8.0, 26.0
Please indicate how much you are concerned about inducing further harm associated with NOT treating blood glucose concentrations $>$ 10 mmol/L in patients with diabetes? (70 ^b)		
Yes, this is a major concern	4 (6%)	1.6, 14.0
Yes, but not a major concern	48 (68%)	56.4, 79.1
No, it is not a concern	18 (26%)	16.0, 37.6
The results of NICE-SUGAR have impacted blood glucose concentrations I target in the ICU. (71 ^b)		
Strongly agree	27 (38%)	26.8, 50.3
Agree	28 (39%)	28.0, 51.7
Neutral	12 (17%)	9.0, 27.7
Disagree	2 (3%)	0.3, 9.8
Strongly disagree	2 (3%)	0.3, 9.8
There is currently sufficient evidence to determine the optimal blood glucose range for patients with T2DM admitted to the ICU. (70 ^b)		
Strongly agree	2 (3%)	0.3, 9.9
Agree	15 (21%)	12.5, 32.9

Table 2 (continued)

Clinical scenarios and response options	Responses n (%) ^a	CI
Neutral	16 (23%)	13.7, 34.4
Disagree	26 (37%)	25.9, 49.5
Strongly disagree	11 (16%)	8.1, 26.4
I would be prepared to enrol ICU patients with T2DM into a randomised trial of liberal blood glucose control (10–14 mmol/L). (71 ^{b,c})		
Strongly agree	17 (23%)	14.6, 35.5
Agree	28 (39%)	28.0, 51.7
Neutral	14 (20%)	11.2, 30.9
Disagree	9 (13%)	6.0, 22.7
Strongly disagree	3 (4%)	0.9, 11.9
I am concerned about the potential for increased risk of infection if T2DM patients only had insulin commenced for blood glucose concentrations \geq 14 mmol/L (71 ^b)		
Strongly agree	4 (6%)	1.6, 13.8
Agree	29 (41%)	29.3, 53.2
Neutral	24 (34%)	23.0, 46.0
Disagree	11 (15%)	8.0, 26.0
Strongly disagree	3 (4%)	0.9, 11.9
I am concerned about the potential for hypoglycaemia ($<$ 4.0 mmol/L) when aiming for blood glucose concentrations between 6–10 mmol/L in patients with T2DM (71 ^{b,c})		
Strongly agree	8 (11%)	5.0, 21.0
Agree	25 (35%)	24.2, 47.5
Neutral	13 (18%)	10.1, 29.3
Disagree	23 (32%)	21.8, 44.5
Strongly disagree	2 (3%)	0.3, 9.8
The lowest blood glucose concentration that I think is safe for patients with T2DM to tolerate during ICU admission is (71 ^b)		
Between 6.0 and 10.0 mmol/L	41 (58%)	45.4, 69.4
Between 4.0 and 5.9 mmol/L	27 (38%)	26.8, 50.3
Between 3.0 and 3.9 mmol/L	3 (4%)	0.9, 11.9
Between 2.3 and 2.9 mmol/L	0 (0%)	0.0, 5.1
Please select the specific patient groups you would be willing to enrol into a liberal blood glucose concentrations study for T2DM patients (tick all that apply). (54 ^{b,d})		
Cardiothoracic	32 (59%)	45.0, 72.4
Neurosurgical	32 (59%)	45.0, 72.4
Elective surgery	43 (80%)	66.5, 89.4
Trauma	40 (74%)	60.3, 85.0
Medical	53 (98%)	90.1, 100
Do you think it would be feasible to have two glucose protocols one for patients with and one for without diabetes? (71 ^b)		
Strongly agree	7 (10%)	4.1, 19.3
Agree	38 (53%)	41.3, 65.5
Neutral	11 (15%)	8.0, 26.0
Disagree	11 (15%)	8.0, 26.0
Strongly disagree	4 (6%)	1.6, 13.8

NICE-SUGAR, Normoglycaemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation; ICU, intensive care unit.

^a Percentage of the total number of responses for that question.^b Number of responses.^c Percentage may not total 100 because of rounding.^d Respondents could pick multiple each could total 100.

4.3. Future research

Additional studies are required to establish the current practices for managing critically ill patients with T2DM; different study methodologies may provide a more robust reflection of practice. The exploration of global blood glucose management practice of critically ill T2DM patients is the area that could be explored to understand how ANZ compares different regions.

5. Conclusion

Australian and New Zealand intensivists remain uncertain about optimal blood glucose targets in patients with T2DM, with half of the respondents feeling that there is insufficient evidence for blood glucose management in patients with T2DM. Presently, the majority (93%) would aim for the NICE-SUGAR targets of between 6.0 and 10.0 mmol/L with 87% commencing intravenous insulin to

achieve these targets. Within our sample, there was sufficient equipoise to support conducting a trial evaluating a more liberal approach to blood glucose control in ICU patients with T2DM.

CRedit authorship contribution statement

Alexis Poole: conceptualised the project, managed and coordinated the project, assisted with design of methodology, analysed data, prepared the initial and final drafts of the manuscript. **Glenn Eastwood:** conceptualised the project, assisted with management and coordination for the project, assisted with design of methodology, contributed to reviewing and commenting on the initial and final drafts of the manuscript. **James Anstey, Rinaldo Bellomo, Vishwanath Biradar, Adam M. Deane, Simon R. Finfer, Mark E. Finnis, Craig J. French, Palash Kar, Peter S. Kruger, Matthew J. Maiden, Johan Mårtensson, Colin J. McArthur, Shay P. McGuinness, Paul J. Secombe, Antony E. Tobin and Andrew A. Udy:** assisted with management and coordination for the project, assisted with design of methodology, contributed to reviewing and commenting on the initial and final drafts of the manuscript.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.aucc.2018.09.001>.

Ethical approval

This survey was approved by the Royal Adelaide Hospital Human Research Ethics Committee.

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