CUMULATIVE TIME IN BAND (cTIB): GLYCEMIC LEVEL, VARIABILITY AND PATIENT OUTCOME ALL IN 1

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Introduction – Objectives – Methods – Results – Conclusion

- Glycemic variability
- Extreme BG levels repetition
- Extreme BG levels exposure

ICU mortality
Introduction – Objectives – Methods – Results – Conclusion

Glycemic Control (GC)

- Glycemic variability
- Extreme BG levels repetition
- Extreme BG levels exposure

ICU mortality
But...

Does it work?
Introduction – Objectives – Methods – Results – Conclusion

But...

Does it work?


GC implementation difficulties

- Hypoglycemic risk
  - Safety
- Glycemic target band
  - Efficiency
- GC performance assessment in real time
  - Quality
Insight on issues that impede GC implementation

1) Can GC positively impact on ICU mortality?

2) Is there a glycemic target band performance metric or level that can be assessed in real time that ensures and discriminates improved patient outcome?

3) When should glycemic control performance be assessed?
Introduction – Objectives – Methods – Results – Conclusion

Patient Data

<table>
<thead>
<tr>
<th></th>
<th>SPRINT¹</th>
<th>Glucontrol²</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>784</td>
<td>933</td>
<td>1717</td>
</tr>
<tr>
<td>Percentage of males</td>
<td>61.2</td>
<td>63.2</td>
<td>62.3</td>
</tr>
<tr>
<td>Age of patients</td>
<td>65.0 [52.0 - 74.0]</td>
<td>65.2 [51.5 - 74.0]</td>
<td>65.0 [51.8 - 74.0]</td>
</tr>
<tr>
<td>APACHE 2 score</td>
<td>18.0 [15.0 - 24.0]</td>
<td>15.0 [11.0 - 21.0]</td>
<td>17.0 [13.0 - 23.0]</td>
</tr>
<tr>
<td>Cohort BG (mmol/L)</td>
<td>6.2 [5.3 - 7.4]</td>
<td>6.9 [5.8 - 8.4]</td>
<td>6.6 [5.6 - 8.1]</td>
</tr>
<tr>
<td>Per-patient median BG (mmol/L)</td>
<td>6.3 [5.6 - 7.5]</td>
<td>6.9 [6.1 - 8.2]</td>
<td>6.6 [5.8 - 7.9]</td>
</tr>
<tr>
<td>%BG in 4-7 mmol/L</td>
<td>66.8</td>
<td>49.8</td>
<td>56.4</td>
</tr>
</tbody>
</table>

Data are in the form of median [inter-quartile range, IQR] where applicable.


Percentage of blood glucose levels within a specific glycemic band from start to the present day

- Calculated per day and per patient
- Accounts for BG levels and variability
- Measures glycemic outcome and control performance
• Intermediate levels
• $\Delta = 3$ mmol/L

• Intermediate levels
• $\Delta = 3$ mmol/L

• Intermediate levels
• $\Delta = 4$ mmol/L
Patient Data → Daily cTIB → cTIB threshold

cTIB ≥ t

t = 50%, 60%, 70%, 80%
Introduction – Objectives – **Methods** – Results – Conclusion

Patient Data $\rightarrow$ Daily cTIB $\rightarrow$ cTIB threshold

**cTIB $\geq t$**

$t = 50\%, 60\%, 70\%, 80\%$

- **cTIB = 32.8%**
  - Mean BG : 7.4 mmol/L

- **cTIB = 65.6%**
  - Mean BG : 6.9 mmol/L

- **cTIB = 83.6%**
  - Mean BG : 6.3 mmol/L
Patient Data → Daily cTIB → cTIB threshold

cTIB ≥ t

t = 50%, 60%, 70%, 80%

cTIB = 32.8% < 50%
Mean BG : 7.4 mmol/L

cTIB = 65.6% ≥ 50%
Mean BG : 6.9 mmol/L

cTIB = 83.6% ≥ 50%
Mean BG : 6.3 mmol/L

Mean BG : 7.4 mmol/L

Mean BG : 6.9 mmol/L

Mean BG : 6.3 mmol/L

cTIB in 4.0 – 7.0 mmol/L
Introduction – Objectives – Methods – Results – Conclusion

Patient Data → Daily cTIB → cTIB threshold

cTIB ≥ t

t = 50%, 60%, 70%, 80%

cTIB = 32.8% < 70%
Mean BG : 7.4 mmol/L

cTIB = 65.6% < 70%
Mean BG : 6.9 mmol/L

cTIB = 83.6% ≥ 70%
Mean BG : 6.3 mmol/L
**Patient Data**

- **cTIB = 32.8%**
  - Mean BG: 7.4 mmol/L

- **cTIB = 65.6%**
  - Mean BG: 6.9 mmol/L

- **cTIB = 83.6%**
  - Mean BG: 6.3 mmol/L

**cTIB ≥ t**

- **t = 50%, 60%, 70%, 80%**
Patient Data → Daily cTIB → cTIB threshold

\[ cTIB \geq t \]

\( t = 50\%, 60\%, 70\%, 80\% \)

→ different levels of GC performance

→ discrimination of improved outcomes
Introduction – Objectives – Methods – Results – Conclusion

Ratio between odds of living given cTIB ≥ t and odds of living given cTIB < t

<table>
<thead>
<tr>
<th>ICU mortality</th>
<th>Lived</th>
<th>Died</th>
</tr>
</thead>
<tbody>
<tr>
<td>cTIB ≥ t</td>
<td>N₁</td>
<td>N₂</td>
</tr>
<tr>
<td>cTIB &lt; t</td>
<td>N₃</td>
<td>N₄</td>
</tr>
</tbody>
</table>

\[
OL_{cTIB \geq t} = \frac{N_1}{N_2} \\
OL_{cTIB < t} = \frac{N_3}{N_4}
\]

\(N_i\) : number of patients.
ICU mortality

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\[
\begin{align*}
OL_{cTIB \geq t} &= \frac{N_1}{N_2} \\
OL_{cTIB < t} &= \frac{N_3}{N_4}
\end{align*}
\]

\[
OR = \frac{OL_{cTIB \geq t}}{OL_{cTIB < t}} = \frac{N_1 \cdot N_4}{N_2 \cdot N_3}
\]

\[
CI_{95\%} = \left[ e^{\ln(OR) - 1.96 \sqrt{\frac{1}{N_1} + \frac{1}{N_2} + \frac{1}{N_3} + \frac{1}{N_4}}} , e^{\ln(OR) + 1.96 \sqrt{\frac{1}{N_1} + \frac{1}{N_2} + \frac{1}{N_3} + \frac{1}{N_4}}} \right]
\]
Glycemic levels

cTIB in **4.0-7.0 mmol/L** vs. cTIB in **5.0-8.0 mmol/L**
Glycemic levels

cTIB in **4.0-7.0 mmol/L** vs. cTIB in **5.0-8.0 mmol/L**

cTIB ≥ 50%
Glycemic levels

\textbf{cTIB in 4.0-7.0 mmol/L vs. cTIB in 5.0-8.0 mmol/L}

\begin{itemize}
  \item \textbf{cTIB in 4.0-7.0 mmol/L} vs. \textbf{cTIB in 5.0-8.0 mmol/L}
\end{itemize}
Glycemic levels
cTIB in 4.0-7.0 mmol/L vs. cTIB in 5.0-8.0 mmol/L
Glycemic levels

cTIB in **4.0-7.0 mmol/L** vs. cTIB in **5.0-8.0 mmol/L**

→ 4.0-7.0 mmol/L


Glycemic variability

cTIB in **4.0-7.0 mmol/L** vs. cTIB in **4.0-8.0 mmol/L**
tighter vs. wider glycemic band
Glycemic variability

cTIB in 4.0-7.0 mmol/L vs. cTIB in 4.0-8.0 mmol/L
tighter vs. wider glycemic band
Glycemic variability

cTIB in 4.0-7.0 mmol/L vs. cTIB in 4.0-8.0 mmol/L

tighter vs. wider glycemic band
**Introduction – Objectives – Methods – Results – Conclusion**

**Glycemic variability**

cTIB in **4.0-7.0 mmol/L** vs. cTIB in **4.0-8.0 mmol/L**
tighter vs. wider glycemic band

→ **4.0-7.0 mmol/L**

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Glycemic control performance
When can it be assessed?
Glycemic control performance
When can it be assessed?

- cTIB ≥ 50%
- cTIB ≥ 60%
- cTIB ≥ 70%
- cTIB ≥ 80%
Glycemic control performance
When can it be assessed?

→ After 3 days


Introduction – Objectives – Methods – Results – Conclusion

1) Can GC positively impact on ICU mortality?

Yes ...

(1) Association

max. BG within an intermediate glycemic band
= increased OR = improved patient outcomes

(2) Causation

Previous randomized control trials 1,2

Physiological reasons 3 + others


2) Is there a glycemic target band performance **metric** or level that can be assessed in real time that ensures and discriminates improved patient outcome?

Yes...

cTIB

- 1 metric to assess glycemic levels, glycemic variability and patient outcomes
- 1 metric able to reproduce different previous results about GC assessment
- 1 metric easily calculated in real-time
→ 1 metric to rule them all!
2) Is there a glycemic target band performance metric or level that can be assessed in real time that ensures and discriminates improved patient outcome?

Yes...

4.0-7.0 mmol/L = increased OR = improved patient outcome

- BG < 7.0 mmol/L = increased OR
- No hypo (BG < 4.0 mmol/L) = increased OR
3) When should glycemic control performance be assessed?

After 3 days...

Lower CI bound < 1.0 for Days 1-3
Thank you for your attention

Questions?