Impact of glucose meter error on efficacy of glycemic control after cardiovascular surgery

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Disclosures

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Outline

• **Introduction**
  o Glucose meter use in the hospital
  o Glycemic control and hypoglycemia
  o Glucose meter accuracy guidelines

• **Glucose meter error and glycemic control efficacy**
Glucose meters in the hospital

- Multiple uses for glucose meters in hospital
  - Dose subcutaneous insulin for diabetic mildly ill patients
    - Same accuracy requirements as home use
  - Screen for neonatal hypoglycemia
  - Screen for hypoglycemia or hyperglycemia in hospitalized patients
  - Manage intravenous insulin for critically ill patients on glycemic control
    - Hourly glucose measurement, hourly IV insulin adjustment
    - Narrower insulin dosing ranges, more opportunity for dosing errors
Glucose meters in the hospital

• Number of factors influence relationship of glucose meter to true (usually lab plasma) glucose
  o Whole blood vs. plasma (conversion factor)
    − Influenced by hematocrit, plasma water, red cell water
    − Assumptions based upon healthy population
    − Safe assumption in home, not so much in hospital
  o Sample type (capillary vs. venous catheter vs. arterial catheter)
    − Physiologic and technologic limitations
  o Interferences (medications, pO2, others)
## Glucose meters in hospital

### Error and outliers with WB glucose

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sample type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock, hypotension, dehydration, edema</td>
<td>Capillary</td>
</tr>
<tr>
<td>Hematocrit effect</td>
<td>All</td>
</tr>
<tr>
<td>Failure to let alcohol dry</td>
<td>Capillary</td>
</tr>
<tr>
<td>Underdosing strips</td>
<td>Capillary, All</td>
</tr>
<tr>
<td>PW or RW effect</td>
<td>All, CVC &gt; art line?</td>
</tr>
<tr>
<td>Medication interference</td>
<td>All</td>
</tr>
<tr>
<td>pH, O2 or CO2 tension</td>
<td>All? CVC?</td>
</tr>
<tr>
<td>Use of expired or incorrectly stored strips</td>
<td>All</td>
</tr>
<tr>
<td>Temperature extremes</td>
<td>All</td>
</tr>
<tr>
<td>Incorrect calibration info</td>
<td>All</td>
</tr>
<tr>
<td>Improper/incorrect disinfection</td>
<td>All</td>
</tr>
<tr>
<td>Operator error/untrained operators</td>
<td>All</td>
</tr>
</tbody>
</table>
Glucose meters in the hospital

• With all these limitations, what is motivating the desire to measure glucose and adjust insulin doses at the bedside?
  o Recognition of harm of hyperglycemia in the ICU, especially diabetic patients after cardiovascular surgery
  o Glycemic control with intravenous insulin as major trend in critical care
  o Turn-around time limitations of lab glucose, harm of delayed insulin dose adjustment when given intravenously
    – Speed vs. accuracy (limitations)
Glycemic control vs. hypoglycemia

- **Leuven 1, Van den Berghe 2001**
  - First large trial tight glycemic control (TGC) surgical ICU
  - Primary findings:
    - Among patients in ICU > 5 days, mortality reduced ~ 30% in intensive insulin group
    - Increased rate of hypoglycemia in intensive group (6x, 5% of intensive group)
    - ABG analyzers used to measure blood glucose

- **Leuven II, Van den Berghe 2006**
  - Repeat of study in medical ICU
  - TGC only effective in patients with > 3 d ICU stay
  - Hypoglycemia significant limitation, increased mortality for patients < 3 d in ICU
  - 6-fold increased rate of hypoglycemia (18.7%)
  - Glucose meters instead of ABG
**Glycemic control vs. hypoglycemia**

- Single episode of severe hypoglycemia (< 40 mg/dL) associated with increased mortality
  - OR 2.3 X for death (Krinsley, 2007)

- In same population patients glycemic control reduced mortality

- Sensitivity analysis performed to determine how much SH would offset TGC
  - 4X increase in SH (from 2.3% to 9.2%) predicted to completely offset survival benefit of TGC
Glycemic control vs. hypoglycemia

• TGC protocols associated with 5-14 X increase incidence of hypoglycemia

• Absolute rates of hypoglycemia vary widely between TGC studies depending on target and protocol
  o 0.34% (Stamford Hospital)
  o 18.7 % (Leuven II)

• Does the glucose meter error have anything to do with glycemic control outcomes or rate hypoglycemia?

• What is required accuracy of glucose meters used to manage glycemic control?
Glucose meter accuracy guidelines

• ISO 15197 (2013) and NACB (2011)
  o 95% of glucose meter results within...
    - ±15 mg/dL (0.83 mM) at glucose < 100 mg/dL
    - ±15% at glucose ≥ 100 mg/dL (5.56 mM)
    - 99% within zones A&B on consensus error grid (ISO)

• CLSI POCT 12-A3
  o 95% glucose meter results within...
    - ±12 mg/dL (0.67 mM) at glucose < 100 mg/dL
    - ±12.5% at glucose ≥ 100 mg/dL (5.56 mM)
    - 98% within ±20% (≥100 mg/dL) or 15 mg/dL (<100 mg/dL)

• American Diabetes Association
  o ±10% of true value for all devices for all purposes (home use, hospital use), ±5% of true value is ideal
Glucose meter accuracy in the hospital

• Differing total error recommendations—10-15%  
• Can “newer” glucose meter technologies achieve 10-15% total error when fresh whole blood samples are tested on critically ill patients after cardiovascular surgery?  
  – If so, because bias or imprecision is reduced?  
  – Where are we at today, how did we get there (reducing bias or reducing imprecision)  
• Does reducing glucose meter error improve efficacy of glycemic control in the cardiovascular ICU?  
  – Does it matter?
Measuring glucose meter accuracy in the ICU

- Nova StatStrip replaced Roche AccuChek Inform 10/2012
- Assess impact on accuracy and precision of glucose measurements in ICU
  - Accuracy when routine clinical samples tested at bedside
    - Retrospective study with Inform and StatStrip
  - Precision with fresh arterial whole blood from critically ill patients
Measuring glucose meter accuracy in the ICU

- Precision (prospective study)

- Roche AccuChek Inform (20 ICU patients with 5x measurement at the bedside)
  - CV of 2.0% at an average glucose value of 142 mg/dL (7.89 mM)

- Nova StatStrip (20 ICU patients with 5x measurement at the bedside)
  - CV of 2.7% at an average glucose value of 140 mg/dL (7.78 mM)

- Both meters precise when fresh whole blood tested at bedside
Measuring glucose meter accuracy in the ICU

• **Accuracy (retrospective study)**
  
  o Over 3 month period, 1602 Inform whole blood glucose measurements performed within 5 minutes of drawing serum glucose (Roche Hexokinase)
  
  o Over separate 3 month period, 1093 StatStrip whole blood glucose performed within 5 minutes of serum glucose
Measuring glucose meter accuracy in the ICU

- Median bias 11 mg/dL (0.61 mM)
- Median (IQR) % bias 9 (4 to 14) %
Measuring glucose meter accuracy in the ICU

- Median bias 1 mg/dL (0.06 mM)
- Median (IQR) % bias 1 (-3 to 5) %
## Results—glucose meter accuracy in ICU

<table>
<thead>
<tr>
<th></th>
<th>Inform (n=1602)</th>
<th>StatStrip (n=1093)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent within 10% lab</td>
<td>55%</td>
<td>89%</td>
</tr>
<tr>
<td>Percent with 20% lab</td>
<td>92%</td>
<td>98%</td>
</tr>
<tr>
<td>% within 15%/15 mg/dL (NACB, new ISO 15197) serum</td>
<td>80%</td>
<td>97%</td>
</tr>
<tr>
<td>% within 12.5%/12.5 mg/dL (CLSI POCT12-A3) serum</td>
<td>69%</td>
<td>95%</td>
</tr>
</tbody>
</table>

- By reducing bias, reduced TEa from ~20% ← 12.5%
Impact of insulin dosing errors on glycemic control in ICU

- **Impact on patient outcome**
  - ICU/hospital mortality
  - Hospital morbidity (infections, transfusions, renal failure)
  - Requires randomized trial > 1000 patients

- **Impact on glycemic control efficacy**
  - Glycemic variability
  - Time within target range
  - Incidence hypo and hyperglycemia
  - Requires 50-150 patients per study arm
Impact of insulin dosing errors on glycemic control in ICU

- Why measure glycemic control efficacy?
  - Hypoglycemia important outcome
  - Hyperglycemia is what is being avoided
  - Glycemic variability
    - More variability = more hypo and hyperglycemia
    - Increased variability (extreme highs and lows) may alone decrease survival in ICU
  - ↑ time in target range, ↓ hypo and hyperglycemia, ↓ variability = better protocol
  - Can reducing meter error alone lead to a better protocol?
Study design

- Given improved accuracy of meter in ICU
  - ~20% → 12.5% TEa

- Can we measure impact on glycemic control efficacy?

- Retrospective review patients post cardiovascular surgery placed on glycemic control in CVS ICU
  - 12-24 consecutive (30-120 min) glucose values on insulin drip
  - Period 1 (70 patients monitored with AccuChek Inform)
  - Period 2 (70 patients monitored with StatStrip)
  - No change infusion protocol, testing personnel, etc
Study design

- **Measures glycemic variability**
  - Standard deviation (SD)
  - Continuous overall net glycemic action (CONGA)
  - Percent values in target range (110-150 mg/dL)
  - Incidences of hypoglycemia and hyperglycemia

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD age (range)</td>
<td>68 ± 12 (28-92)</td>
<td>65 ± 12 (29-86)</td>
<td>0.22</td>
</tr>
<tr>
<td>Gender</td>
<td>39 M/ 31 F</td>
<td>42 M/ 28 F</td>
<td>0.61</td>
</tr>
<tr>
<td>Diabetes</td>
<td>35 ND/ 35 T2DM</td>
<td>35 ND/ 35 T2DM</td>
<td></td>
</tr>
<tr>
<td>Median (range) number glucose values</td>
<td>22 (12-24)</td>
<td>21 (12-24)</td>
<td>0.16</td>
</tr>
</tbody>
</table>
Results—Glycemic variability and time within target range

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (n=70)</th>
<th>Period 2 (n=70)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR) glucose (mg/dL)</td>
<td>141 (126, 156)  mg/dL</td>
<td>136 (125, 148) mg/dL</td>
<td>0.005</td>
</tr>
<tr>
<td>Median (IQR) standard deviation (SD)</td>
<td>21.6 (16.9, 26.3) mg/dL</td>
<td>13.7 (12.4, 19.1) mg/dL</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Median (IQR) CONGA</td>
<td>19.4 (16.0, 24.2) mg/dL</td>
<td>13.5 (10.9, 17.3) mg/dL</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Median (IQR) percent values in target range (%)</td>
<td>66.7 (50, 74.2) %</td>
<td>74.5 (58.5, 86.7) %</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Glycemic variability decreased and time in target range increased with improved meter accuracy
### Results—Glycemic variability and time within target range

**Non-diabetic patients only**

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (n=35)</th>
<th>Period 2 (n=35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median (IQR) standard deviation (SD)</strong></td>
<td>18.7 (16.3, 25.6) mg/dL</td>
<td>15.4 (12.4, 19.9) mg/dL</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Median (IQR) CONGA</strong></td>
<td>18.3 (13.3, 21.6) mg/dL</td>
<td>13.5 (10.2, 19.0) mg/dL</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Median (IQR) time in target range (%)</strong></td>
<td>68.8 (61.9, 79.2)</td>
<td>73.7 (62.5, 87.5)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

- Glycemic variability (SD and CONGA) decreased ~ 20%
- No significant change in time in target range
## Results—Glycemic variability and time within target range

- **Type 2 diabetes only**

<table>
<thead>
<tr>
<th></th>
<th>Period 1 (n=35)</th>
<th>Period 2 (n=35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median (IQR) standard deviation (SD)</strong></td>
<td>22.4 (17.7, 28.0) mg/dL</td>
<td>13.6 (12.3, 18.3) mg/dL</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Median (IQR) CONGA</strong></td>
<td>21.4 (18.3, 27.5) mg/dL</td>
<td>13.5 (11.7, 15.2) mg/dL</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Median (IQR) time in target range (%)</strong></td>
<td>61.9 (46.7, 72.7) %</td>
<td>78.3 (54.2, 85.7) %</td>
<td>0.006</td>
</tr>
</tbody>
</table>

- ~40% decrease in glycemic variability (SD and CONGA)
- ~25% increase in time in target range

**Bigger impact on patients with Type 2 diabetes**
Results—Incidence of hypo and hyperglycemia

- **Hypoglycemia** (< 70 mg/dL, 3.89 mM)
  - 1 patient, 1 value Period 1
  - 0 patients, 0 values Period 2

- **Hyperglycemia** (> 200 mg/dL, 11.11 mM)
  - 26 patients (7 non-diabetic and 19 T2DM), Period 1
  - 6 patients (1 non-diabetic and 5 T2DM), Period 2
Conclusions

• Glucose meter use in the hospital
  o Often done on non-diabetic patients
  o Tighter glucose ranges, more opportunities to “translate” glucose measure error into insulin dosing error
  o Sources of error (hematocrit, medication interferences, sample type differences) more pronounced effects

• Newer glucose meter technologies reduce error of glucose measurement when used at the bedside on critically ill patients

• Evidence emerging that improving glucose meter performance (reducing error) will improve efficacy of glycemic control
Questions?