MAYO CLINIC

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

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Disclosures

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Outline

- Introduction
  - Glucose meter use in the hospital
  - Glycemic control and hypoglycemia
  - 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**
  - **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*
  - **Sample type (capillary vs. venous catheter vs. arterial catheter)**
    - *Physiologic and technologic limitations*
  - **Interferences (medications, pO2, others)**

Glucose meters in hospital

- **Error and outliers with WB glucose**

Condition	Sample type
Shock, hypotension, dehydration, edema	Capillary
Hematocrit effect	All
Failure to let alcohol dry	Capillary
Underdosing strips	Capillary, All
PW or RW effect	All, CVC > art line?
Medication interference	All
pH, O2 or CO2 tension	All? CVC?
Use of expired or incorrectly stored strips	All
Temperature extremes	All
Incorrect calibration info	All
Improper/incorrect disinfection	All
Operator error/untrained operators	All

Glucose meters in the hospital

- **With all these limitations, what is motivating the desire to measure glucose and adjust insulin doses at the bedside?**
  - **Recognition of harm of hyperglycemia in the ICU, especially diabetic patients after cardiovascular surgery**
  - **Glycemic control with intravenous insulin as major trend in critical care**
  - **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
  - 0.34% (Stamford Hospital)
  - 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)**
  - **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**
  - **95% glucose meter results within…**
    - *± 12 mg/dL (0.67mM) 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 (< 100mg/dL)*
- **American Diabetes Association**
  - **± 10% of true value for all devices for all purposes (home use, hospital use), ± 5% of true value is idea**

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**

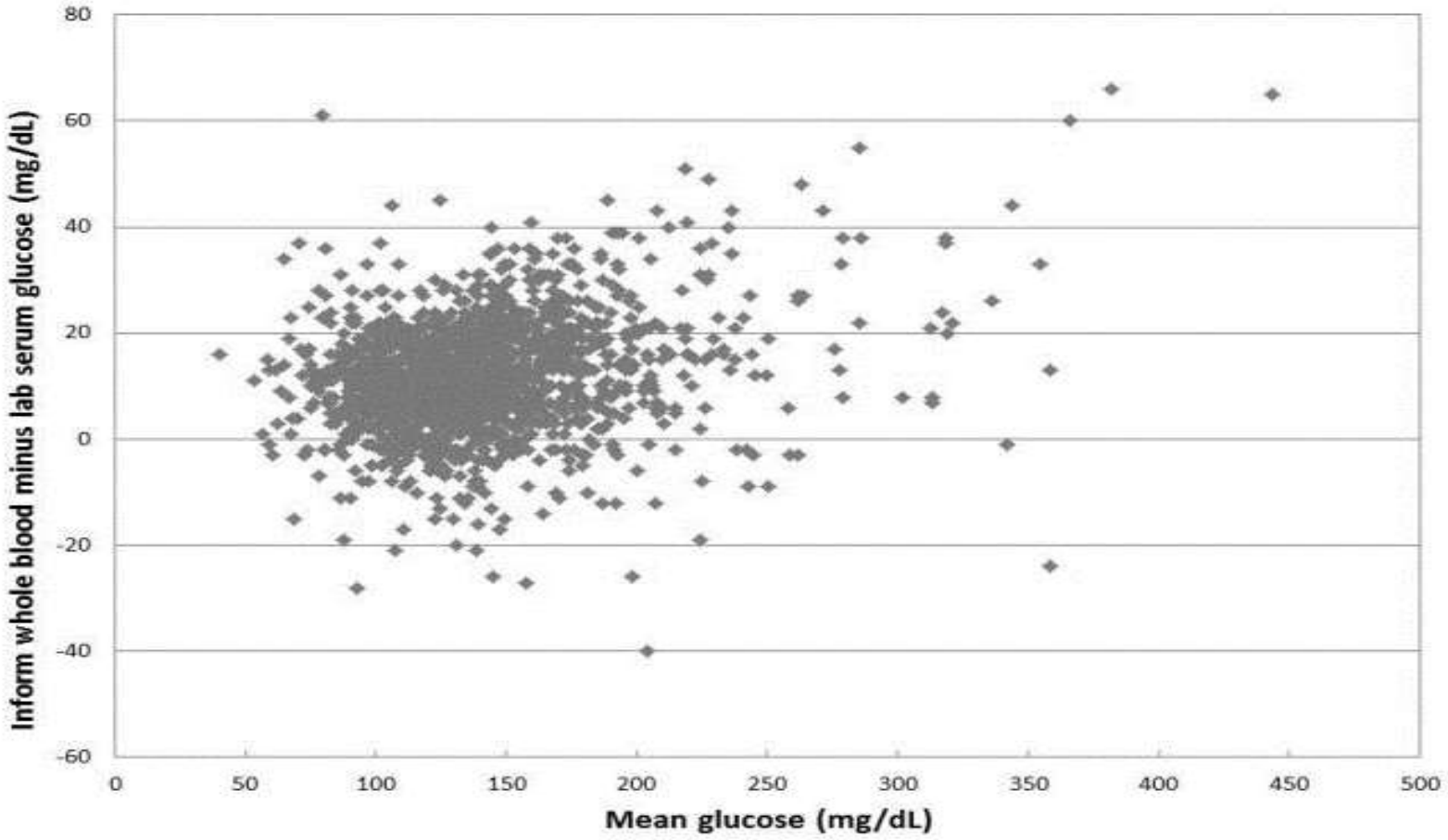
Measuring glucose meter accuracy in the ICU

- **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

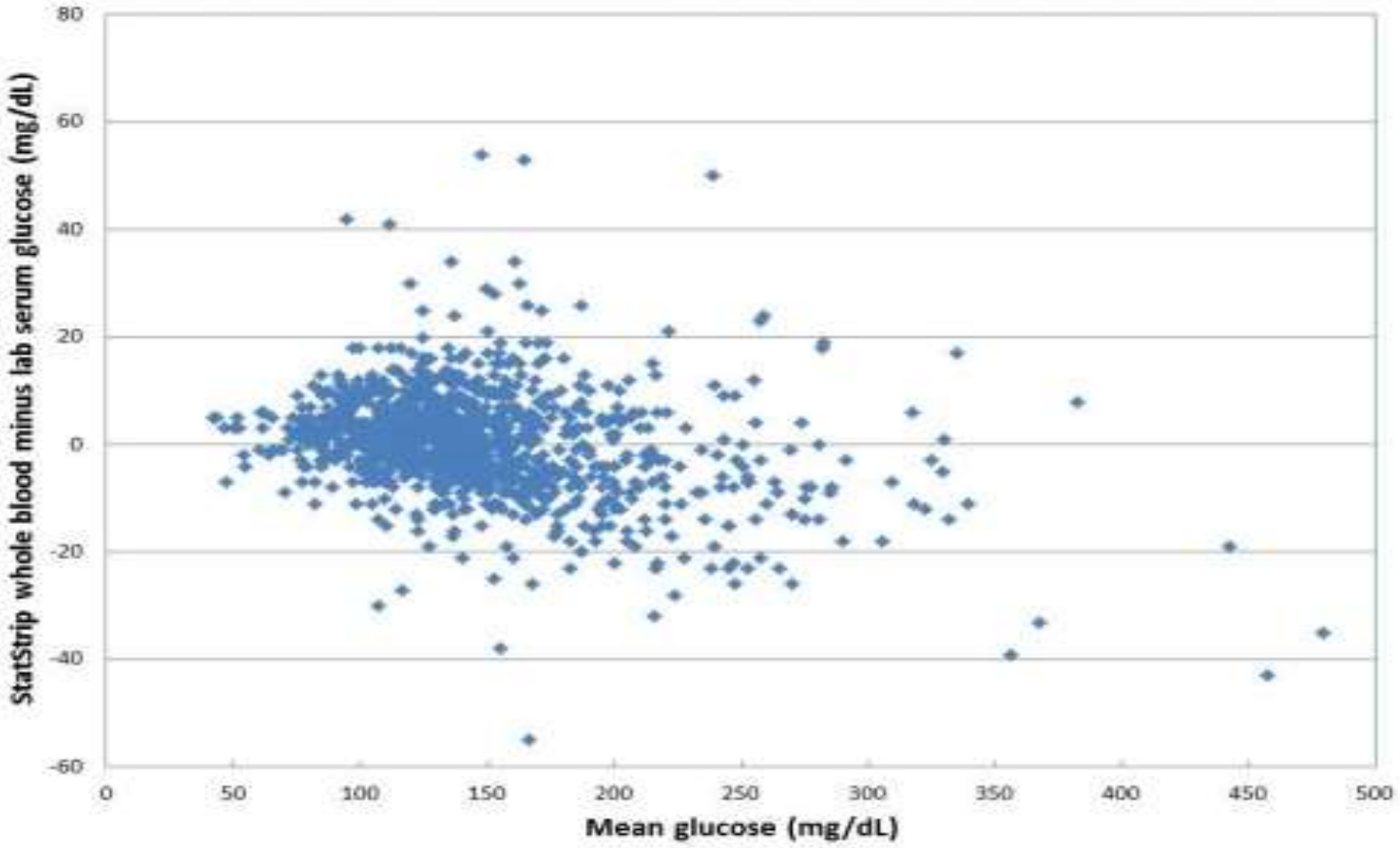
- **Accuracy (retrospective study)**
  - **Over 3 month period, 1602 Inform whole blood glucose measurements performed within 5 minutes of drawing serum glucose (Roche Hexokinase)**
  - **Over separate 3 month period, 1093 StatStrip whole blood glucose performed within 5 minutes of serum glucose**

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

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

- **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**

Patient demographics	Period 1 (6-11/2012)	Period 2 (8/13-2/14)	P value
Mean ± SD age (range)	68 ± 12 (28-92)	65 ± 12 (29-86)	0.22
Gender	39 M/ 31 F	42 M/ 28 F	0.61
Diabetes	35 ND/ 35 T2DM	35 ND/ 35 T2DM	
Median (range) number glucose values	22 (12-24)	21 (12-24)	0.16

Results—Glycemic variability and time within target range

- **Overall results (non-diabetic and T2DM)**

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

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**

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

- 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**

	Period 1 (n=35)	Period 2 (n=35)	P value
Median (IQR) standard deviation (SD)	**22.4** (17.7, 28.0) mg/dL	**13.6** (12.3, 18.3) mg/dL	<0.0001
Median (IQR) CONGA	**21.4** (18.3, 27.5) mg/dL	**13.5** (11.7, 15.2) mg/dL	<0.0001
Median (IQR) time in target range (%)	**61.9** (46.7, 72.7) %	**78.3** (54.2, 85.7) %	0.006

- ~ 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**
  - **Often done on non-diabetic patients**
  - **Tighter glucose ranges, more opportunities to "translate" glucose measure error into insulin dosing error**
  - **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?