SUPPLEMENTARY DATA

Supplementary Table 1. Insulin Treatment Protocols:

1. Basal Bolus Regimen with Insulin Glargine and Glulisine
1.A. Insulin Orders
• Discontinue oral antidiabetic drugs (sulfonylureas, repaglinide, nateglinide, metformin, pioglitazone, rosiglitazone, sitagliptin) and non-insulin injected antidiabetic medication (pramlinitide, exenatide) on admission.
• Starting insulin total daily dose (TDD): 0.5 units per kg of body weight.   • Reduce insulin TDD to 0.3 units per kg of body weight in patients ≥ 70 years of age and/or with a serum creatinine ≥ 2.0 mg/dL.
• Give half of total daily dose as insulin glargine and half as insulin glulisine.
• Give insulin glargine once daily, at the same time of the day.
• Give insulin glulisine in three equally divided doses before each meal. Hold insulin glulisine if patient not able to eat.
1.B. Supplemental insulin
• Give supplemental insulin glulisine following the "sliding scale" protocol (1E) for blood glucose > 140 mg/dl.
• If a patient is able and expected to eat all, give supplemental glulisine insulin before each meal and at bedtime following the "usual" column.
• If a patient is not able to eat, give supplemental glulisine insulin every 6 hours (6-12-6-12) following the "sensitive" column.
1.C. Insulin adjustment
• If the fasting and predinner BG is between 100 - 140 mg/dl in the absence of hypoglycemia the previous day: no change
• If the fasting and predinner BG is between 140 - 180 mg/dl in the absence of hypoglycemia the previous day: increase insulin TDD by 10% every day
• If the fasting and predinner BG is >180 mg/dl in the absence of hypoglycemia the previous day: increase insulin TDD dose by 20% every day
• If the fasting and predinner BG is between 70 - 99 mg/dl in the absence of hypoglycemia: decrease insulin TDD dose by 10% every day
• If a patient develops hypoglycemia (BG <70 mg/dL), the insulin TDD should be decreased by 20%.
1.D. Blood glucose monitoring. Blood glucose will be measured before each meal and at bedtime (or every 6 hours if a patient is not eating) using a glucose meter

1.E. Supplemental Insulin Scale

Blood Glucose (mg/dL)	☐ Insulin Sensitive	☐ Usual	☐ Insulin Resistant
141-180	2	4	6
181-220	4	6	8
221-260	6	8	10
261-300	8	10	12
301-350	10	12	14
351-400	12	14	16
> 400	14	16	18

** Check appropriate column below and cross out other columns

The numbers in each column indicate the number of units of glulisine or regular insulin per dose. Supplemental" dose is to be added to the scheduled dose of glulisine or regular insulin.

2. Regular Insulin By Sliding Scale

2.A. Insulin Orders

- Discontinue oral antidiabetic drugs (sulfonylureas, repaglinide, nateglinide, metformin, pioglitazone, rosiglitazone, sitagliptin) and non-insulin injected antidiabetic medication (pramlinitide, exenatide) on admission.

- **Patients who are not eating or with intermittent nutritional intake**

  - If a patient is not able to eat or if the nutritional intake is uncertain/intermittent, regular insulin will be administered every 6 hours following the "insulin sensitive" recommended dose of the sliding scale protocol (2D).

- **Patients who are eating**

  - If a patient is able and expected to eat most of his/her meals, regular insulin will be administered before each meal and at bedtime following the "usual" recommended dose of the sliding scale protocol.
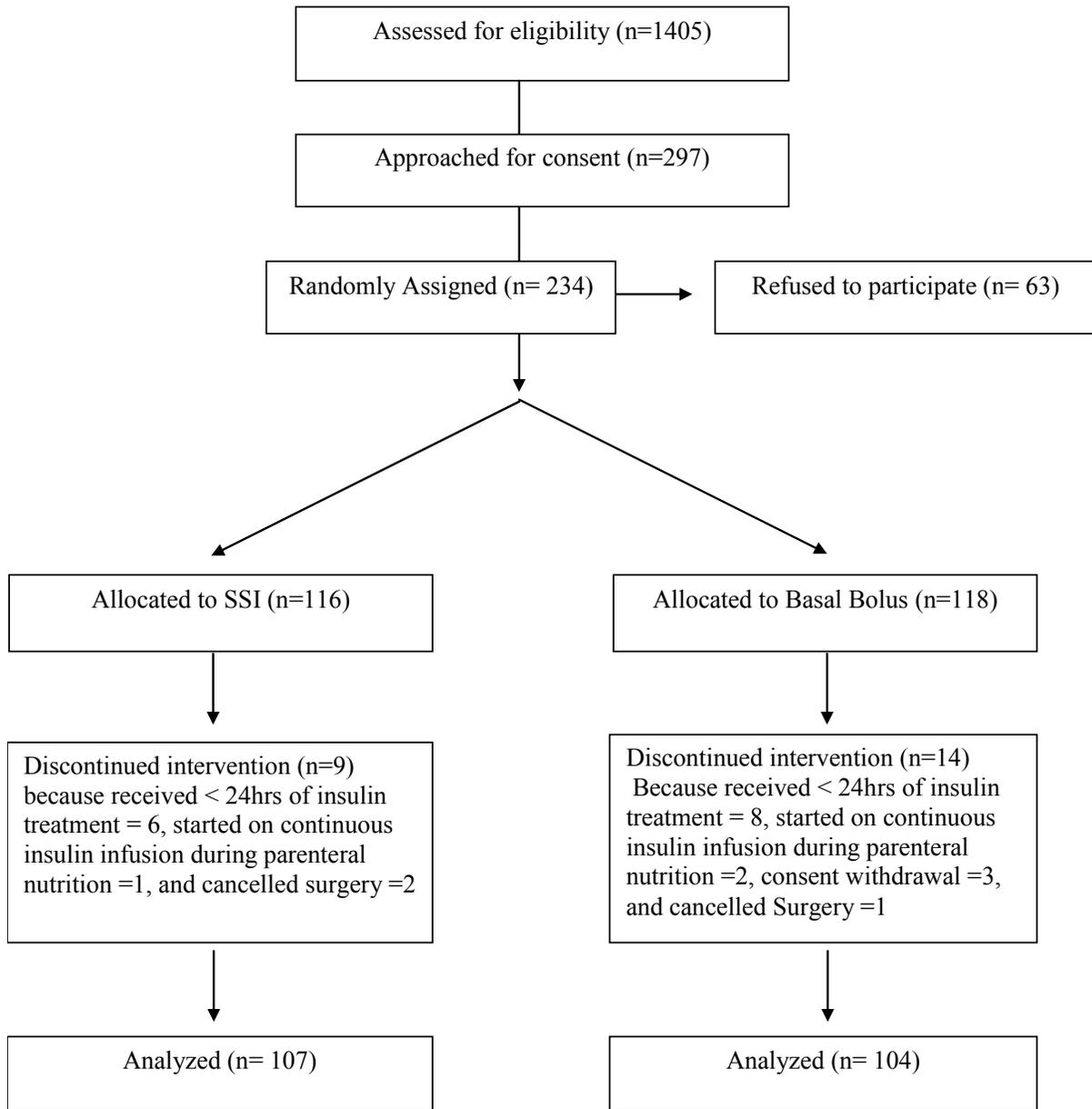
2.B. Insulin adjustment

- If the fasting and pre-meal plasma glucose are persistently >140 mg/dL in the absence of hypoglycemia, the insulin scale of regular insulin could be increased from sensitive to usual, or from the usual to resistant scale.

- If a patient develops hypoglycemia (blood glucose <60mg/dL), the sliding scale of regular insulin should be decreased from insulin resistant to usual scale or from the usual to sensitive scale.

2.C. Blood glucose monitoring. Blood glucose will be measured before each meal and at bedtime (or every 6 hours if a patient is not eating) using a glucose meter.

2.D. Sliding Scale Regular Insulin

	☐	☐	☐
Blood Glucose (mg/dL)	Insulin Sensitive	Usual	Insulin Resistant
141-180	2	4	6
181-220	4	6	8
221-260	6	8	10
261-300	8	10	12
301-350	10	12	14
351-400	12	14	16
> 400	14	16	18

** Check appropriate column below and cross out other columns

The numbers in each column indicate the number of units of glulisine or regular insulin per dose. Supplemental" dose is to be added to the scheduled dose of glulisine or regular insulin.

SUPPLEMENTARY DATA

Supplementary Figure 1. Patients in the study.

Adult patients admitted to undergo elective or emergency and non-cardiac surgery and who were assumed not to require ICU admission were eligible for inclusion.
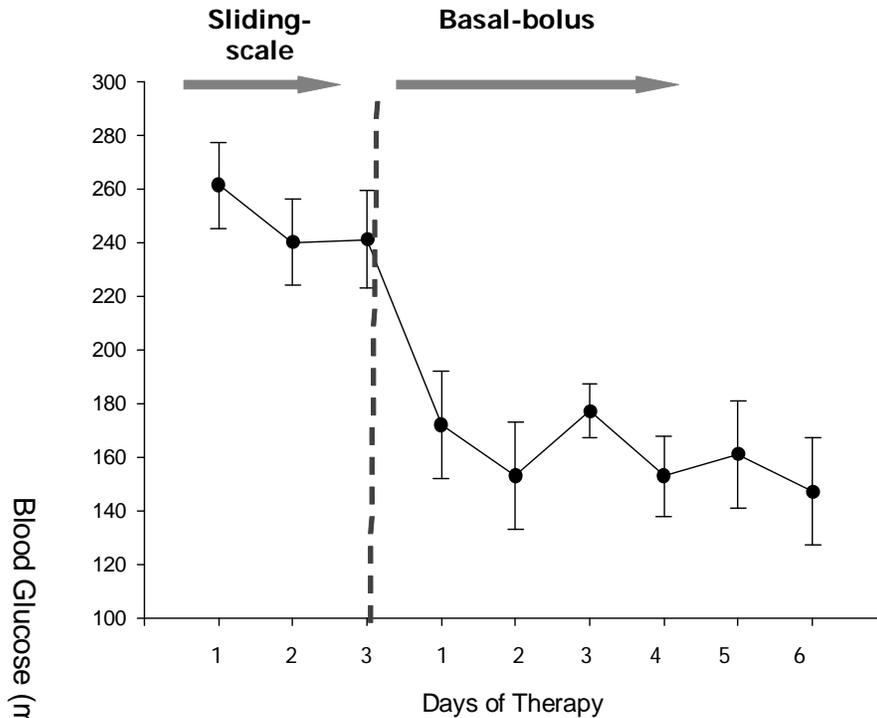
<u>RABBIT 2 SURGERY TRIAL</u>

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┌─────────────────────────────────────┐
│  Assessed for eligibility (n=1405)   │
└─────────────────────────────────────┘
                 │
┌─────────────────────────────────────┐
│   Approached for consent (n=297)     │
└─────────────────────────────────────┘
                 │
┌──────────────────────────┐      ┌──────────────────────────────┐
│ Randomly Assigned (n=234)│─────▶│ Refused to participate (n=63)│
└──────────────────────────┘      └──────────────────────────────┘
           │
     ┌─────┴──────┐
     ▼            ▼
┌──────────────────────┐   ┌────────────────────────────────┐
│ Allocated to SSI     │   │ Allocated to Basal Bolus       │
│ (n=116)              │   │ (n=118)                        │
└──────────────────────┘   └────────────────────────────────┘
     │                            │
     ▼                            ▼
┌──────────────────────────┐ ┌────────────────────────────────┐
│ Discontinued intervention│ │ Discontinued intervention      │
│ (n=9) because received   │ │ (n=14) Because received        │
│ < 24hrs of insulin       │ │ < 24hrs of insulin             │
│ treatment = 6, started   │ │ treatment = 8, started on      │
│ on continuous insulin    │ │ continuous insulin infusion    │
│ infusion during          │ │ during parenteral nutrition =2,│
│ parenteral nutrition =1, │ │ consent withdrawal =3,         │
│ and cancelled surgery =2 │ │ and cancelled Surgery =1       │
└──────────────────────────┘ └────────────────────────────────┘
     │                            │
     ▼                            ▼
┌──────────────────────┐   ┌────────────────────────────────┐
│ Analyzed (n= 107)    │   │ Analyzed (n= 104)              │
└──────────────────────┘   └────────────────────────────────┘
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Figure 2 (Appendix): Treatment Failure with Sliding Scale Insulin

Thirteen patients (12%) treated with SSI remained with BG > 240 mg/dL despite increasing the SSI dose to the maximal or insulin resistant scale. Compared to the remaining patients treated with SSI, these patients had a higher mean admission glucose (242±95 mg/dL vs. 175±74 mg/dL, p= 0.127) and developed higher rate of wound infection (30.8 % vs. 7.5%, p=0.027).

12 patients (14%) treated with SSI had persistent severe hyperglycemia (3 consecutive BG>240 mg/dl). Patients were switched to basal bolus regimen.