

Table S1. Characteristics of insulin regimens and nutritional support in the studies included in the systematic review.

Author, Year	Insulin Regimen 1	Insulin Regimen 2	Insulin Regimen 3	Nutritional Support
ENTERAL NUTRITION				
Randomized Control Trials				
Korytkowski 2009	Sliding scale regular insulin every 4-6 h according to bedside glucose monitoring. NPH insulin was added if persistent glucose > 180 mg/dl	Insulin glargine plus sliding scale regular insulin	None	No protocol. % of total energy: CHO 34-65% The majority of patients received formulas using ≥50% CHO
Leelarathna 2013	Fully automated IV regular insulin: sc continuous glucose monitoring systems, computer running a model predictive control algorithm, and two syringe pumps (one with insulin solution and the other with 20% dextrose infusion)	Local insulin therapy paper-based protocol: glucose goal values: 72-360 mg/dl. Insulin infusion titrated according to bedside glucose monitoring. Hourly infusion rates adjusted by the attending physician if glucose was outside target	None	Local protocol. One patient received both enteral and parenteral nutrition. Mean Energy: 63.2kcal/h Mean CHO: 7.5 g/hour
Cohort Studies				
Grainger 2007	Fixed dose of glargine insulin and variable doses of lispro insulin. Daily glargine according to BMI: <30 kg/m ² - 10 UI; ≥30 kg/m ² - 20 UI. Baseline lispro dose according to BMI and CHO feeding: <30 kg/m ² , 1UI for every 15g of CHO; BMI ≥30 kg/m ² , 1 UI for every 10g of CHO. Baseline lispro titrated according to glucose monitoring.	Preprandial insulin prescribed by the house-staff physician.	None	Two feeding formulas: TwoCal HN (standard formula): 200kcal/100ml, protein 8.35 g/100ml, CHO 21.9/100ml; Nepro (renal failure): 200kcal/ml, protein 7 g/100ml, CHO 22.27g/100ml. Energy needs were estimated on actual body weight depending on BMI. Tube feeding was given by bolus every 4 h. No continuous drip-enteral feeding
Cook 2009	SC sliding scale of aspart insulin. Insulin titrated according to: UI of insulin = (BG - 100)/20	NPH insulin sliding scale every 4h. Insulin titrated on daily basis according to predefined table.	NPH insulin sliding scale every 6h. Insulin was titrated daily according to predefined table.	Continuous enteral feeding using 9 different types of formulas. Energy goal: all patients received at least 70% of calculated basal energy expenditure.
Hsia 2011	Basal bolus glargine/lispro. Lispro administered as needed at 6h intervals if BG >180 mg/dl.	Premixed insulin 70/30 twice daily. Lispro administered as needed at 6h intervals if BG >180 mg/dl.	Premixed insulin 70/30 3 times daily. Lispro administered as needed at 6h interval if BG >180 mg/dl.	Primary team and nutritional service decided about type of enteral nutrition and caloric content Continuous enteral feeding. CHO: 45- 65% of total energy.

Dickerson 2013	Transition from continuous IV regular human insulin to s.c. NPH insulin using intermittent IV supplemental regular insulin. Initial NPH dose: 30%-50% of continuous insulin in the previous 24h, divided into 2 separate doses and given every 12 h.	Transition from IV intermittent regular human insulin to s.c. NPH using intermittent IV supplemental regular insulin. NPH insulin therapy added to preexisting intermittent corrective IV regular insulin approach.	None	“Diabetic” enteral formula (lower in CHO and higher lipid content) or specialized (glutamine/ ω 3 fatty or fluid restricted) Continuous enteral nutrition..
Murphy 2013	A 70/30 premixed human insulin was prescribed at beginning of the feed.	Short acting s.c. insulin before each feed plus glargine insulin at night.	Once or twice daily prescription of long acting insulin analogue	All patients were fed with a standard 1kcal/ml formula to meet nutritional requirements Nutrition support according to insulin regimen: continuous enteral feed over 20h or intermittent bolus feeding lasting over 4h

PARENTERAL NUTRITION

Randomized Control Trials

Hakeam 2015	Glargine insulin was initiated in a dose equal to 80% of the total insulin received through rapid insulin sliding scale (RISS) on the previous day; thereafter, adjustments were based on laboratory MBG: 141-216 mg/dl: 40% of total RISS; >216 mg/dl: 60% of total RISS; <70 mg/dl: next insulin dose reduced by 50%	Regular insulin added in PN solution in a dose equal to 80% of the total insulin received through rapid insulin sliding scale on the previous day; adjustments were based on laboratory measured BG: 141- 216 mg/dl: 40% of total RISS; >216 mg/dl: 60% of total RISS; <70 mg/dl: next insulin dose reduced by 50%	None	Individualized PN formula in a 2-in-1 fashion through a central IV line. PN target goal was achieved on day 3, providing macronutrients based on: 1.5 g/kg for amino acids; 2 mg/kg/min, for dextrose; and 168-240 mL for lipids. All PN started at 21:00 at 50ml/h. Caloric characteristics ~20kcal/kg.
Oghazian 2015	In the glargine insulin group dose was 80% of total daily dose of regular insulin used in PN solution on the day prior to randomization. Glargine insulin was administered 2h before next PN infusion.	If BG was already in 151 to 199 mg/ dl range, 0.15 units of insulin per gram of dextrose were added on the 1 st day; if BG measured on the day before starting PN was 121-150, 100-120, and <100 mg/dl, 10, 5, and 0 units of insulin per gram of dextrose were added in PN bag, respectively. If needed, regular insulin was also administered s.c. to correct any glucose values >150 mg/dl according to a correctional insulin dosing protocol (correctional protocol provides 2 units of regular insulin for every 50 mg/ dl of blood glucose over 150 mg/dl. Subsequently, 70-100% of the correctional insulin dose is added to the next day PN solution.		PN provides approximately 40–60% of calculated daily energy requirement of CHO during the first 24h (150 to 250g of dextrose) and is then promoted to the desired goal during the next 24 hours. IV amino acid and fat emulsion are started from day 1 based on individualized requirements.

Jakoby 2012	For patients without diabetes, insulin was started as 1U/20 g CHO. Prandial regular insulin was administered in PN (2/3 of total insulin) and basal NPH insulin (1/3 of total insulin) in 4 equal sc doses at 6-hour interval. For patients with diabetes and initial BG measure <200 mg/dl, prandial insulin was administered as 1U/10 g CHO and basal insulin as NPH 0.15U/kg/day in 4 doses of 6h-hour interval. For patients with diabetes and initial BG >200 mg/dl prandial regular insulin was 1U/5 g CHO and basal NPH insulin was 0.25U/kg/day. Insulin adjustments followed a predefined protocol.	Patients who met the eligibility criteria and were managed before the implementation of insulin protocol and treated with sliding scale insulin	None	Nutrient content of PN and infusion rates were left at the discretion of the pharmacist. Patients were excluded if >10% of daily CHO was delivered through the alimentary tract.
Neff 2014	Patients with hyperglycemia while on PN were started with a IV insulin protocol.	Patients with hyperglycemia were individually prescribed s.c. insulin with no standardized dose. Patients received a mixture of rapid acting insulin analog and basal insulin.	None	Not described

MIXED NUTRITIONAL SUPPORT

Randomized Control Trials

Holzinger 2004	Patients received a continuous infusion of 1UI/h of insulin during 24 hours.	Patients received a saline infusion of 1ml/h during 24 hours.	None.	All patients received artificial nutrition continuously via parenteral and/or enteral routes during the study. Daily energy needs were calculated as 25 kcal per kg of total body weight.
Van Herpe 2013	The insulin dosage is guided by software. The model comprises information regarding patient profile (reason for ICU admission, BMI, history of diabetes, severity of illness) and other variables such as BG, insulin dose sequence, and steroid medication).	The insulin dosage is defined by a paper guideline.	None.	Patients received dextrose 5% 30-40 ml/h as long as 7 days after ICU admission. Enteral nutrition was started when possible, and if enteral nutrition was insufficient at 7 days in ICU, PN was initiated on day 8 to reach energy goal.

Cohort studies

Thomas 2005	No standardized doses of insulin. The resident prescribed an insulin sliding scales to achieve blood glucose control.	Insulin protocol that used a calculator to define insulin dose.	Modified web-based insulin protocol: amount was increased by an extra 1U/h above the values produced by the old protocol when BG was >130 mg/dl plus a bolus of 2U of insulin.	Feeding protocol: a daily intake of approximately 1800 calories.
Dortch	BG was managed with an automated nurse driven, computer based protocol. The bedside nurse enters the BG, the	BG was manually managed by nurse driven, paper based protocol. The nurse calculated the	None	Primary glucose source, consisting of dextrose containing fluids that delivered a partial CHO supply of 5-10g/h. As soon

2007	primary source of glucose and method of glucose measurement. The computer software calculates the recommended insulin dose .	recommend dose of insulin according to an algorithm.		as possible PN, combined PN and enteral or enteral feeding was instituted. Enteral feeding the preferred support nutrition.
Dickerson 2014	Former algorithm recommending Aggressive titration of insulin infusion to maintain blood glucose 100 – 125 mg/dl	New algorithm allowed a slower progression of insulin	None	Patients received continuous enteral feeding or PN. Daily target for caloric intake was 30 to 35 kcal/kg and for protein 0.8 to 1.5 g/kg based on serum urea nitrogen concentration or changes in serum nitrogen concentration between dialysis periods. If enteral or PN was discontinued, to prevent hypoglycemia a 5% dextrose solution was started at the same infusion rate as the feeding formulation.

BG = blood glucose; BMI = body mass index; CHO = carbohydrate; IV = intravenous; PN = parenteral nutrition; s.c. = subcutaneous