ADDITIONAL FILE 1

Dysglycemias in patients admitted to ICUs with severe acute respiratory syndrome due to COVID-19 versus other causes – A cohort study

Rosângela Roginski Réa[1,2], Rafaella Stradiotto Bernardelli[2-3], Amanda Christina Kozesinski-Nakatani[2,4], Marcia Olandoski[3], Marcelo José Martins-Junior[2], Mirella Cristine de Oliveira[2,5], Álvaro Réa-Neto[1,2].

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Table S1 - Characteristics of patients from each of the eight participating sites (hospitals).

VARIABLES	HOSPITALS (sites)							
	HR (n=210)	HT (n=198)	HSC (n=160)	HIM (n=116)	HVB (n=80)	HMC (n=74)	HN (n=32)	INC (n=1)
Baseline								
Diagnoses								
Non-COVID-19	13 (6.2)	27 (16.1)	12 (7.5)	43 (37.1)	18 (22.5)	15 (20.3)	9 (28.1)	1 (100)
COVID-19	197 (93.8)	141 (83.9)	148 (92.5)	73 (62.9)	62 (77.5)	59 (79.7)	23 (71.9)	0 (0)
Age (years)	59.1 ± 14.7	57.2 ± 15.7	65 ± 16.5	64 ± 15.8	58 ± 17.7	62.4 ± 20	67.6 ± 16.5	80 ± 0
Male sex	111 (52.9)	99 (58.9)	91 (56.9)	59 (50.9)	50 (62.5)	45 (60.8)	14 (43.8)	1 (100)
History of diabetes	44 (26.2)	72 (34.3)	56 (35)	40 (34.5)	21 (26.3)	18 (24.3)	8 (25)	0 (0)
Presumed obesity	70 (41.7)	88 (41.9)	19 (11.9)	30 (25.9)	18 (22.5)	20 (27)	5 (15.6)	0 (0)
Charlson Comorbidity Index	1 (0 - 1)	1 (0 - 1)	1 (0.5 - 2)	1 (0 - 2)	1 (0 - 2)	1 (0 - 2)	1 (0 - 1)	3 (3 - 3)
ICU admission status								
APACHE II score in the first 24hrs in ICU	11.5 (7 - 18)	13 (8 - 20)	19 (12 - 28)	11 (7 - 17)	11 (5 - 16.5)	14 (10 - 18)	11.5 (6 - 17.5)	20 (20 - 20)
SOFA score in the first 24 hrs in ICU	3 (2 - 6)	3 (2 - 6)	5 (3 - 7)	4 (3 - 6)	3 (2 - 5)	3 (2 - 6)	3 (2 - 4.5)	13 (13 - 13)
CRP level in the first 24 hrs in the ICU[a]	110 (57 - 173.5)	122 (71.5 - 183.5)	138.9 (84.1 - 199)	109 (30.7 - 177.5)	79.5 (31.5 - 134.5)	108.5 (52 - 165)	77 (51 - 129)	122 (122 - 122)
Related to glycemic abnormalities in the ICU								
Highest glucose value at ICU admission[b]	172.5 (132 - 255)	169.5 (139.5 - 219)	146 (113.5 - 222)	158 (122 - 225)	152.5 (114.5 - 201)	138 (112 - 195)	146.5 (116 - 169)	108 (108 - 108)
Highest glucose value during ICU stay	251.5 (180 - 388)	242.5 (175 - 387.5)	226 (154 - 366.5)	254.5 (167 - 376.5)	203.5 (136.5 - 363.5)	236 (161 - 361)	176 (150 - 298.5)	153 (153 - 153)
Mean glucose value during ICU stay	156.2 (132.2 - 218.1)	144.4 (123.4 - 195)	138.5 (111.7 - 183.1)	152.2 (122.9 - 213.6)	137.4 (110.9 - 173.3)	148.8 (123 - 195.8)	124.4 (106.9 - 171.5)	130.5 (130.5 - 130.5)
Mean glucose variability (CV %) during ICU stay[c]	23.4 (18.4 - 34.2)	25.3 (18.8 - 36.3)	35.4 (24.2 - 51.3)	31.6 (22.3 - 43.1)	25.6 (17.8 - 36.3)	31.5 (24.8 - 42.9)	25.1 (20 - 37.7)	. (. - .)

	HT	HR	HSC	IMP	HVB	HMC	HN	INC
% of days with hyperglycemia (≥180 mg/dL)	50 (7.1 - 90)	34.2 (0 - 81.8)	33.3 (0 - 84.5)	50 (0 - 87.5)	25 (0 - 65.2)	23.2 (0 - 76.5)	0 (0 - 47.7)	0 (0 - 0)
Occurrence of hypoglycemia (<70 mg/dL) during ICU stay	34 (16.2)	42 (25)	77 (48.1)	36 (31)	14 (17.5)	10 (13.5)	5 (15.6)	0 (0)
Related to progression within 30 days of ICU stay								
Nosocomial infection	41 (24.4)	55 (26.2)	20 (12.5)	15 (12.9)	19 (23.8)	14 (18.9)	5 (15.6)	0 (0)
Mean SOFA score during ICU stay	4 (2.2 - 6.4)	3.6 (2 - 6.6)	6 (3.3 - 8.5)	5.3 (3.3 - 7.3)	3 (2 - 5.8)	3 (2 - 5.6)	2.8 (1.9 - 7)	14 (14 - 14)
Mean CRP level during ICU stay[a]	133.5 (74.7 - 185.7)	125.2 (61.4 - 179.2)	154.2 (82.9 - 202.7)	111.2 (60.5 - 181)	79.5 (43.9 - 132.6)	105.7 (66.7 - 152.8)	93.3 (46 - 143.8)	210 (210 - 210)
Use of corticosteroid during ICU stay	96 (57.1)	151 (71.9)	102 (63.8)	109 (94)	41 (51.3)	39 (52.7)	13 (40.6)	0 (0)
ICU length of stay	8 (4 - 20)	6 (3 - 10)	5 (2 - 9)	6 (4 - 12)	4 (2 - 10)	7 (4 - 15)	5 (2.5 - 10)	1 (1 - 1)
30 days ICU mortality	73 (34.8)	48 (28.6)	84 (52.5)	66 (56.9)	22 (27.5)	17 (23)	9 (28.1)	1 (100)

Data are expressed as number (percent), mean ± standard deviation, or median (first quartile - third quartile).

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; CRP, C-reactive protein (mg/L); VAD: vasoactive drug; IMV: invasive mechanical ventilation. The glucose values are shown as mg/dL; hrs: hours; CV, Coefficient of variation.

Abbreviations for the names of the hospitals: HT, Hospital do Trabalhador; HR, Hospital de Reabilitação; HSC, Hospital Santa Casa de Curitiba; IMP, Instituto de Medicina do Paraná; HVB, Hospital Vita Batel; HMC, Hospital Marcelino Champagnat; HN, Hospital das Nações; and INC, Instituto de Neurologia de Curitiba.

[a] 2 missing data in the HR; 1 missing data in the HSC; 1 missing data in the HN.

[b] 4 missing data in the IM.

[c] 10 missing data in the HT; 16 missing data in the HR; 2 missing data in the HSC; 4 missing data in the IM; 2 missing data in the HVB; 36 missing data in the HMC; 5 missing data in the HN; and 1 missing data in the INC.

Table S2. Influence of COVID-19 on occurrence of hypoglycemia (<70 mg/dL) during ICU stay unadjusted and adjusted for the variables sex, history of diabetes, presumed obesity, age, APACHE II scores, SOFA scores, CRP levels, and corticosteroid use.

Factors associated with the occurrence of hypoglycemia (<70 mg/dL) during ICU stay	n[$]	OR (95% CI) unadjusted[†]	p value[§]	n[$$]	OR (95% CI) adjusted[††]	p value[§]
COVID-19 [a]	841	1.084 (0.711 - 1.654)	0.707	837	0.856 (0.539 - 1.36)	0.510
Male sex [b]	841	0.843 (0.618 - 1.149)	0.279		-	-
History of diabetes [c]	841	1.941 (1.406 - 2.678)	0.000		1.906 (1.339 - 2.712)	0.000
Presumed obesity [d]	841	0.764 (0.54 - 1.083)	0.130		0.7 (0.475 - 1.03)	0.070
Charlson Comorbidity Index	841	1.188 (1.066 - 1.324)	0.002		-	-
Age	841	1.017 (1.007 - 1.027)	0.001		1 (0.988 - 1.011)	0.972
APACHE II scores	841	1.048 (1.032 - 1.065)	0.000		1.011 (0.991 - 1.031)	0.288
Nosocomial infection [e]	841	2.952 (2.069 - 4.211)	0.000		2.178 (1.478 - 3.209)	0.000
Mean SOFA during ICU stay	841	1.269 (1.202 - 1.339)	0.000		1.191 (1.103 - 1.287)	0.000
Mean CRP during ICU stay	837	1.006 (1.004 - 1.008)	0.000		1.001 (0.999 - 1.004)	0.342
Use of corticosteroid during ICU stay [f]	841	1.187 (0.854 - 1.65)	0.307		- BIC: 907.242[‡]	-

[$] number of cases (n) included in each univariate model.

[$$] number of cases (n) included in the multivariate model; [§] Wald test p value, results <0.05 indicate statistical significance.

[§]Wald test p value, p < 0.05 indicates statistical significance.

[‡] Bayesian information criterion (BIC) of the multivariate generalized linear model, representative of the quality of the model given its explanatory potential, with the lower the BIC, the more the model is able to explain the dependent variable.

[†] Odds ratio (OR) and 95% confidence interval (95% IC) of the generalized linear model with univariate binary logistic distribution.

[††] Odds ratio (OR) and 95% confidence interval (95% IC) of the generalized linear model with multivariate binary logistic distribution.

Table S3 - Adjusted model explaining mortality within 30 days in ICU, including occurrence of hypoglycemia.

Multivariate explanatory models of mortality in the overall cohort	n[#]	OR (95% CI) adjusted*	p value [§]	BIC [‡]
Occurrence of hypoglycemia (<70 mg/dL) during ICU stay (ref: no hypoglycemia)		0.719 (0.422 - 1.227)	0.227	
COVID-19 (ref: non-COVID-19)		2.865 (1.467 - 5.597)	0.002	
History of diabetes (ref: no history)		1.169 (0.699 - 1.958)	0.552	
Age	837	1.016 (1 - 1.033)	0.057	523.057
APACHE II score		1 (0.97 - 1.031)	0.983	
Nosocomial infection (Ref: absent)		1.247 (0.738 - 2.109)	0.409	
Mean SOFA score		2.458 (2.104 - 2.871)	0.000	
Mean CRP level		1.009 (1.006 - 1.013)	0.000	

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; CRP, C-reactive protein (mg/L).

[#] Case numbers included in the model

* Odds ratio (OR) and 95% confidence interval (95% CI) for mortality within 30 days in the ICU, generalized linear models with multivariate binary logistic regression.

[§] Wald test p value, with values <0.05 indicating statistical significance.

[‡] Bayesian information criterion (BIC) of the multivariate generalized linear model representing the quality of the model given its explanatory potential; the lower the BIC, the more the model is able to explain the dependent variable.

Figure S1 - Association between mean glucose levels and 30 days ICU mortality for overall cohort and for each group: COVID-19 and Non-COVID-19