COVID-19 and Diabetes May 13, 2020

- Why does it seem so hard to get a straight story when it comes to COVID-19?
- Diabetes as a risk factor for COVID-19
- Obesity as a risk factor for COVID-19
- Glycemic control and COVID-19 outcomes
- What is the story with ACEI/ARBS



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We usually make recommendations and clinical decisions using evidence from the top of the pyramid

> Right now almost all our information is coming from the bottom of the pyramid



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Diabetes as a risk factor for COVID-19

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Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis

- Studies published from January 1, 2019 to February 25, 2020—all from China
- Diabetes was the 2nd most common comorbidity
- 7 studies met inclusion and exclusion criteria which included 1,576 patients
- Diabetes rates were 9.7%
 (overall Chinese rates 10.7%)

International Journal of Infectious Diseases,Volume 94,2020,Pages 91-95,ISSN 1201-9712,https://doi.org/10.1016/j.ijid.2020.03.017.



Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis



International Journal of Infectious Diseases, Volume 94, 2020, Pages 91-95, ISSN 1201-9712, https://doi.org/10.1016/j.ijid.2020.03.017.

	OR (95% CI)	Eve. severe	Events, Non-seven	% Weight	
-	3.18 (1.95, 5.19)	28/173	53/926	38.08	
	0.25 (0.03, 2.28)	1/13	7/28	10.91	
	- 4.57 (1.46, 14.28)) 8/36	6/102	24.32	
	1.30 (0.47, 3.59)	8/58	9/82	26.70	
	2.07 (0.89, 4.82)	45/280	75/1138	100.00	
	15				
		Events,	Events,	%	
	OR (95% CI)	severe	Non-severe	Weight	
	3.41 (1.53, 7.58)	10/173	17/962	56.05	
\longrightarrow	6.84 (0.26, 179.78)	1/13	0/28	3.34	
•	2.98 (1.11, 7.98)	9/34	11/102	36.78	
	7.30 (0.34, 154.96)	2/58	0/82	3.83	Diabetes
$\langle \rangle$	3.42 (1.88, 6.22)	22/278	28/1174	100.00	
	5				-



Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York City

NYU Langone Health: March 1—April 2 with follow up completed on April 7

Total COVID-19 + population **Preprint** (7,719 tested)	Total COVID (48.7% of to
Median age 52	Median a
50.5% male	62.6% ma
Diabetes—15%	Diabetes
(NYC total diabetes rates about 15%)	Obesity-
Obesity—26.8%	
(NYC total obesity rates 22%)	

- D-19 hospitalized population otal)
- age 62
- nale
- s-31.8%
- -39.8%



Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia: a systematic review, meta-analysis, and meta-regression

- 6452 patients from 30 studies
- Aim of study is to investigate the association of diabetes with poor outcomes in patients with COVID-19 pneumonia

Diabetes & Metabolic Syndrome: Clinical Research & Reviews, Volume 14, Issue 4,2020,Pages 395-403,ISSN 1871-4021,https://doi.org/10.1016/j.dsx.2020.04.018.

Akbari 2020 Bai T 2020 Cao J 2020 Chen 2020 Chen T 2020 Fu L 2020 Li K 2020 Luo XM 2020 Yuan M 2020 Zhou 2020 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.23 Test for overall effect: Z = 6.1.2 Severe COVID-19 Guan 2020 Hu L 2020 Li Q 2020 Liu J 2020 Liu Lei 2020 Ma KL 2020 Qin 2020 Wan 2020 Wang Dan 2020 Wang Y 2020 Yuan B 2020 Zhang Guqin 2020

Study or Subgroup 6.1.1 Mortality

Zhang J 2020 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.1 Test for overall effect: Z =

6.1.3 ARDS

Liu Y 2020 Wu C 2020 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.0 Test for overall effect: Z =

6.1.4 ICU Care

Cao 2020 Huang 2020 Wang D 2020 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.8 Test for overall effect: Z =

6.1.5 Disease Progressio

Feng 2020 Liu W 2020 Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.0 Test for overall effect: Z =

Total (95% CI)

Total events Heterogeneity: Tau² = 0.2 Test for overall effect: Z = Test for subgroup differences: Chi² = 3.24, df = 4 (P = 0.52), l² = 0%

Diabetes Melli	itus (+)	Diabetes Mell	litus (-)		Risk Ratio	Risk Ratio
Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
						10 E 21 E
4	13	29	423	3.6%	4.49 [1.85, 10.91]	
5	36	10	91	3.1%	1.26 [0.46, 3.44]	
6	17	5	85	2.9%	6.00 [2.07, 17.43]	
6	31	8	92	3.2%	2.23 [0.84, 5.91]	
24	113	23	161	5.3%	1.49 [0.88, 2.50]	
26	34	111	166	6.6%	1.14 [0.92, 1.42]	+
7	15	24	87	4.7%	1.69 [0.89, 3.21]	
25	100	32	303	5.5%	2.37 [1.48, 3.79]	
6	10	0	17	0.7%	21.27 [1.32, 341.84]	
17	54	19	137	5.0%	2.27 [1.28, 4.03]	T
	423		1562	40.6%	2.12 [1.44, 3.11]	•
126		261				10A - 1
23; Chi ² = 32.3	31, df = 9 (P = 0.0002); l ²	= 72%			
= 3.82 (P = 0.0	0001)					
28	173	53	926	5.7%	2.83 [1.84, 4.34]	
33	172	14	151	4.9%	2.07 [1.15, 3.72]	
5	26	25	299	3.6%	2.30 [0.96, 5.50]	
3	17	2	44	1.5%	3.88 [0.71, 21.24]	
4	7	0	44	0.7%	50.63 [3.01, 852.14]	· · · · · · · · · · · · · · · · · · ·
7	20	3	64	2.4%	7.47 [2.13, 26.21]	· · · · · ·
53	286	22	166	5.6%	1.40 [0.88, 2.21]	
9	40	3	95	2.4%	7.13 [2.03, 24.95]	· · · · · · · · · · · · · · · · · · ·
9	71	4	72	2.7%	2.28 [0.74, 7.07]	
8	38	7	72	3.4%	2.17 [0.85, 5.52]	
16	92	16	325	4.6%	3.53 [1.84, 6.79]	
7	55	15	166	3.7%	1.41 [0.61, 3.27]	
8	58	9	82	3.6%	1.26 [0.52, 3.06]	
0	1055	5	2506	44.8%	2.45 [1.79, 3.35]	•
190		173				~
	5 df = 12	(P = 0.04); I ² =	45%			
= 5.63 (P < 0.0		(1 - 0.04), 1 -	4576			
- 5.65 (F < 0.6	10001)					
11	53	1	56	1.2%	11.62 [1.55, 86.95]	<u></u>
16	84	6	117	3.5%	3.71 [1.52, 9.09]	
10	137	0	173	4.7%	4.64 [1.86, 11.58]	•
27		7		4.1 /4	104 [100, 1100]	-
	df = 1/P	= 0.29); l ² = 9	¥.			
= 3.29 (P = 0.0		- 0.20), 1 - 0.	10			
- 0.25 (1 - 0.0	,01)					
2	19	13	179	2.0%	1.45 [0.35, 5.95]	
1	13	7	28	1.2%	0.31 [0.04, 2.25]	
8	36	6	102	3.2%	3.78 [1.41, 10.15]	
0	68	0	309	6.4%	1.47 [0.38, 5.67]	-
11		26				
	df = 2/P	= 0.07); l ² = 63	296			
= 0.56 (P = 0.5		- 0.07), 1 - 0.	,,0			
0.00 (1 - 0.0	.,					
ion						
2	15	6	126	1.9%	2.80 [0.62, 12.65]	e <u>ter (ö. 198</u> 7)
2	11	3	67	1.6%	4.06 [0.76, 21.61]	
50	26		193	3.4%	3.31 [1.08, 10.14]	-
4		9			and the second	-
ere eren er) df = 1 (P	= 0.75); l ² = 0	Ma.			
= 2.09 (P = 0.10		- 0.75), 1 0	nd -			
- 2.03 (F = 0.0						
	1709		4743	100.0%	2.38 [1.88, 3.03]	•
358		476			and [1100] 0100]	-
	0 df = 20	(P < 0.00001);	12 - 600/			
= 7.10 (P < 0.0		(r < 0.00001);	- 02%			0.001 0.1 1 10 1000
		(P = 0.52), l ² =	09/			Favours [DM +] Favours [DM -]
nues. Uni* = 3.	$z_{4}, u_{1} = 4$	(r = 0.52), r =	0.70			

Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia: a systematic review, meta-analysis, and meta-regression

Figure 3. Bubble-plot for Meta-regression. Meta-regression analysis showed that the association between diabetes mellitus and composite poor outcome was affected by age [A] and hypertension [B], but not by cardiovascular diseases [C].

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- Single center retrospective cohort study
- Lille, France
- Feb 27–April 5th
- All patients admitted to ICU for COVID-19 were examined
- Primary outcome was need for mechanical ventilation
- 124 patients were admitted to ICU during specified time period
- At time of analysis 48% had been discharged, 15% died and **the rest remained hospitalized
- Comparing COVID-19 patients to controls:
- Median BMI 29.6 to 24—significant
- Age and gender were not significantly different





- Comparing COVID-19 patients to controls:
 - Median BMI 29.6 to 24—significant
 - Age and gender were not significantly different

Simonnet, A., Chetboun, M., Poissy, J., Raverdy, V., Noulette, J., Duhamel, A., Labreuche, J., Mathieu, D., Pattou, F., Jourdain, M. and (2020), High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity. Accepted Author Manuscript. doi:10.1002/oby.22831

a

Patients (%)









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BMI ≥35 kg/m² BMI 30-35 kg/m² BMI 25-30 kg/m² BMI <25 kg/m²





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BMI ≥35 kg/m² (n=35) BMI 30-35 kg/m² (n=24) BMI 25-30 kg/m² (n=48) BMI <25 kg/m² (n=17)



Obesity is associated with severe forms of COVID-19



Similar to previous study but from Lyon, France

- 291 consecutive patients admitted to ICU for SARS-CoV-2
- February 27th and April 8th 2020
- In the Lyon community the rate of obesity was 11.3 %
- Lille rate of obesity 28.2%
- Lille mechanical ventilation rate—68.6%
- Lyon mechanical ventilation rate—58.4%

Caussy, C., Wallet, F., Laville, M. and Disse, E. (2020), Obesity is associated with severe forms of COVID-19. Obesity. Accepted Author Manuscript. doi:10.1002/oby.22842





Obesity in patients younger than 60 years is a risk factor for COVID-19 hospital admission

- Retrospective analysis of BMI stratified by age in COVID-19 positive symptomatic patients who presented to a large academic hospital system in New York City (NYC Langone system)
- March 4th–April 4th

Table 1: Adult patients	who tested positive fo	r Covid-19 March 3-April 4, 20	20 (N= 3,615)		×			
Age ≥ 60 years	N (%)	Admission to acute	P-value	N (%)	ICU Admission	P-value		
	N (70)	(vs discharge from ED)	r-value	N (70)	(vs discharge from ED)	r-value		
BMI 30-34	141 (19%)	0.9 (95% Cl 0.6-1.2)	0.39	57 (22%)	1.1 (95% Cl 0.8-1.7)	0.57		
BMI ≥ 35	99 (14%)	0.9 (95% Cl 0.6-1.3)	0.59	50 (19%)	1.5 (95% CI 0.9-2.3)	0.10		
Age < 60 years								
BMI 30-34	173 (29%)	2.0 (95% 1.6-2.6)	<.0001	39 (23%)	1.8 (95% Cl 1.2-2.7)	0.006		
BMI ≥ 35	134 (22%)	2.2 (95% Cl 1.7-2.9)	<.0001	56 (33%)	3.6 (95% CI 2.5-5.3)	<.0001		

Lighter J, Phillips M, Hochman S, et al. Obesity in patients younger than 60 years is a risk factor for COVID-19 hospital admission. Clin Infect Dis 2020



Obesity in patients younger than 60 years is a risk factor for COVID-19 hospital admission

- BMI 30–34 = 21%, BMI >35 = 16% **Total = 38% obese**
- For patients aged <60 years with a BMI between 30-34:
 - 2.0 times more likely to be admitted to acute care (95% 1.6-2.6, p<0.0001)
 - 1.8 times more likely to be admitted to acute critical care (95% CI 1.2-2.7, p=0.006)
- For patients aged <60 with a BMI >35
 - 2.2 times more likely to be admitted to acute care(95% CI 1.7-2.9, p<.0001)
 - 3.6 times more likely to be admitted to acute and critical care (95% CI 2.5-5.3, p=<.0001)

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Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and **Pre-existing Type 2 Diabetes**

- Retrospective longitudinal, multi-centered study from a cohort of 9,663 confirmed COVID-19 cases enrolled among 19 hospitals in Hubei Province, China
- Initial exclusion left over 7k, of which, 952 had pre-existing diabetes
- Well-controlled BG was defined when glycemic variability ranged from 3.9 to 10.0 mmol/L (70–180 mg/dL). *Total n* = 282
- Poorly-controlled BG was defined when the lowest fasting BG was above or equal 3.9 mmol/L (70 mg/dL) and the highest 2 hPG level exceeded 10.0 mmol/L (180 mg/dL). Total n = 528









Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes



Cell Metabolism,2020,ISSN 1550-4131,https://doi.org/10.1016/j.cmet.2020.04.021.



Figure 3. Survival Curves of Patients with Well-Controlled BG or Poorly Controlled BG



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ACEI or ARB

Yes

???????











Journal of the American Heart Association. 2020;9:e016219



Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes



Cell Metabolism,2020,ISSN 1550-4131,https://doi.org/10.1016/j.cmet.2020.04.021.



Figure 2. Dynamics of BG, Lymphocytes, Neutrophils, IL-6, CRP, and LDH in Well-Controlled and Poorly Controlled BG Groups during Hospitalization



Renin-angiotensin system inhibitors improve the clinical outcomes of COVID-19 patients with hypertension

- 417 patients admitted to hospital in China
 - 51 patients had hypertension
 - 9 patients were excluded for being on no BP meds
 - 42 Patients included in analysis
 - 17 patients treated with ACEI/ARB (5 with comorbidities)
 - 25 patients with non-ACEI/ARB treatment (8 with comorbidities)
- Similar Baseline characteristics
- Blood pressure of all was controlled with current therapy during hospitalization



Renin-angiotensin system inhibitors improve the clinical outcomes of COVID-19 patients with hypertension

- ACEI/ARB group—23% categorized as severe and none died
- nonACEI/ARB group 48% categorized into severe subgroups and one patient died



Not a significant difference





Anti-hypertensive Angiotensin II receptor blockers associated to mitigation of disease severity in elderly COVID-19 patients

- Medical Records from 3 different hospitals in China reviewed
- 78 patients with COVID-19 pneumonia and hypertension included
 - 40 had mild disease and 38 had severe disease
- No significant difference in disease severity with any hypertension medication in the population overall
- In patients over 65 there was a mildly significant decrease in severe disease in patients on ARBS
- Not really convincing either way

Characteristics		Total nationts (n=16)	S	8) Mild patients (n=18) —	Unadjusted			Adjusted		
Characteristics		1 otal patients (n=40)	Severe patients (n=28)		OR	95% CI	p value	OR	95% CI	p value
Antihypertensive use, n(%)										
	No use	8 (17.4)	7 (25)	1 (5.6)	ref		ref	ref		ref
	ССВ	26 (56.5)	18 (64.3)	8 (44.4)	0.791	0.548-1.141	0.403	0.359	0.036-3.58	0.382
	ARB	10 (21.7)	3 (10.7)	7 (38.9)	0.343	0.128-0.916	0.025	0.250	0.064-0.976	0.046
	ACEI	2 (4.3)	1 (3.6)	1 (5.6)	0.571	0.139-2.342	0.378		17 <u></u>	
	Thiazide	3 (6.5)	0 (0)	3 (16.7)						
	BB	7 (15.2)	3 (10.7)	4 (22.2)	0.49	0.2-1.198	0.119			

Table 1. Association between antihypertensive use and disease severity of COVID-19 patients older than 65 years old with hypertension comorbidity

ARB, angiotensin receptor blocker; ACEI, angiotensin converting enzyme inhibitor; CCB, calcium channel blocker; BB, beta blocker. OR, odds ratio; CI, confidence interval.

Adjustment was by multivariable logistic regression modeling with sex variable

Preprint



Bottom Line Advantage vs Disadvantage still uncertain

Don't change med regimen for ACEI/ARB in your patients



Summary

- Unknown if diabetes or obesity increase the risk of getting COVID-19
- Studies are quite consistent that diabetes and obesity increase the risk for poor outcomes with COVID-19
- Mechanisms for increased poor outcomes have yet to be determined but many theories exist and it may be multiple factors
- Glucose control seems to make a difference in outcomes which is not unexpected
- Don't change ACEI or ARB use in your patients due to fears over COVID-19

of **getting** COVID-19 esity increase the risk

