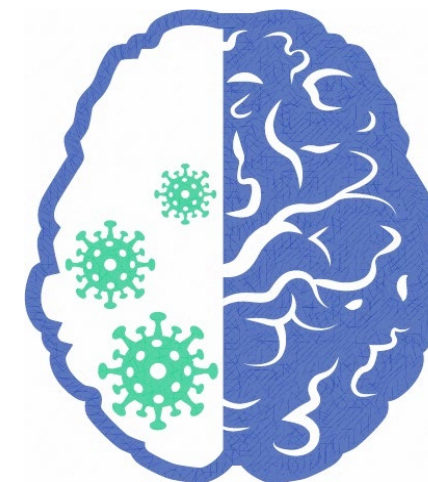


Estudo NeuroCOVID: COVID-19 e as Doenças Cerebrovasculares

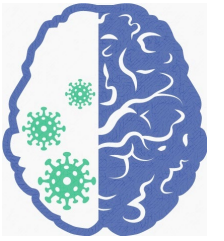
Associação do SARS-CoV-2 com a ocorrência,
o prognóstico e a patogênese das doenças
cerebrovasculares no Brasil



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25 NOVEMBER 2020

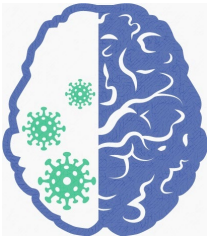
STROKE AND COVID-19: What we know?



Tens of observational studies were published reporting on almost 300 acute stroke cases in patients with COVID-19

Country	IS	ICH	CVST	Total 297	REFERENCES
China	12	2	-	18	Mao et al (JAMA Neurol); Li et al (J Stroke Vasc Neurol); Zhang et al (NEJM)
Qatar	32	-	-	32	Akhtar et al (J Stroke Vasc Neurol)
Iran	3	1	1	5	Sharif-Razavi et al (J Neuro Sciences); Sharif-Razavi et al (NewMicrobes NewInfect); Hemasian et al (Rev Neurol)
Turkey	4	-	-	4	Tunç et al (J Clin Neuroscience)
Dubai	22	-	-	22	Khan et al (Int J Stroke)
Italy	48	5	1	54	Morassi et al (J Neurol); Garaci et al (J Neuro Sciences); Lodigiani et al (Thrombosis Research); Benussi et al (Neurology); Immovilli et al (Int J Stroke)
Spain	1	-	-	1	González-Pinto et al (Eur J Neurol)
France	14	-	-	14	Viguiet et al (J Neuroradiol); Helmes (NEJM); Escalard et al (Stroke)
UK	63	9	1	73	Beyrouti et al (J Neurol Neurosurg Psychiatry); Hughes et al (Eur J Case Reports Int Med); VaraTharaj et al (Lancet Psych)
Netherlands	3	-	-	3	Klok et al (Thrombosis Research)
USA	104	6	5	115	Avula et al (Brain Behav Immun); Saiegh et al (J Neurol Neurosurg Psychiatry); Oxley et al (N Engl J Med); Valderrama et al (Stroke); Reddy et al (Case Rep Neurol); Moshayedi et al (Front Neurol); Sweid et al (Int J Stroke); Yaghi et al (Stroke); Goldberg et al (Am J Neuroradiol); Dakay et al (J Stroke Cerebrovasc Dis); Merckler et al (JAMA Neurol); Patel et al (J Stroke Cerebrovasc Dis)
Brazil	2	4	-	6	Lima et al (Arq Neuropsiq); Estofolete et al (J Med Virol); César-Júnior et al (Int J Stroke)

STROKE AND COVID-19: What we know?



Strokes are being frequently observed in patients with COVID-19, especially critically ill elderly

Many distinct cases (LVO, multiple sites, association with other thromboembolisms and proinflammatory coagulopathy)

Descriptive review of 9 papers
(Munhoz *et al* Arq Neuropsiquiatr May 2020)

Freq of Stroke among patients with COVID-19 = 2.8 – 5.7%

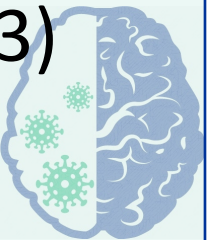
Descriptive review of 17 papers
(Ellul *et al* Lancet Neurology Jun 2020)

Freq of Stroke among patients with COVID-19 = 1.6 – 6%

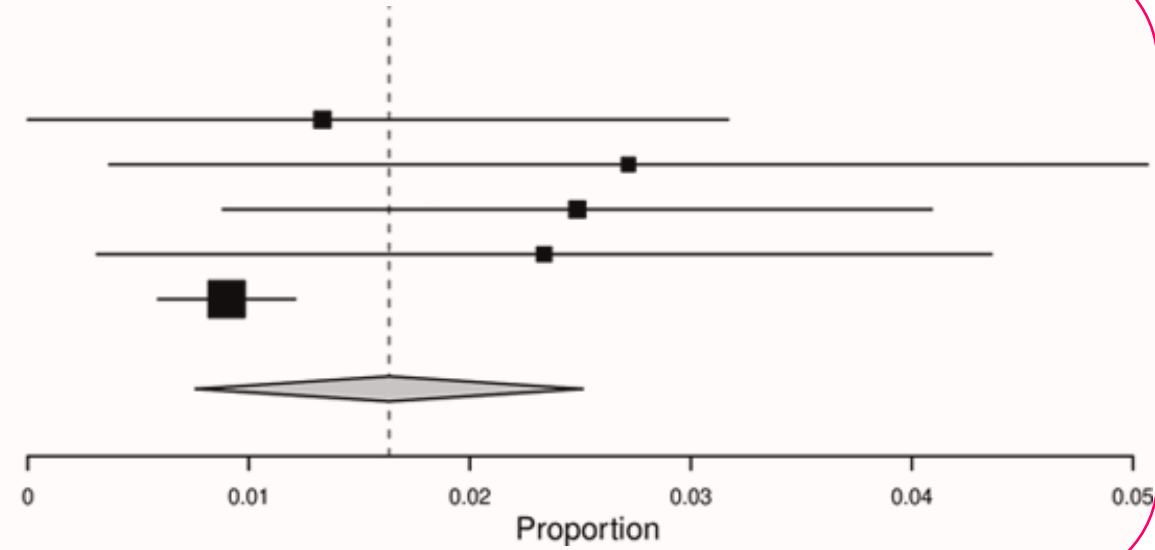
88 ischaemic cases & 8 haemorrhagic cases

Time between COVID and neurologic symptoms = 9.5 days (0-33)

19% of cases died

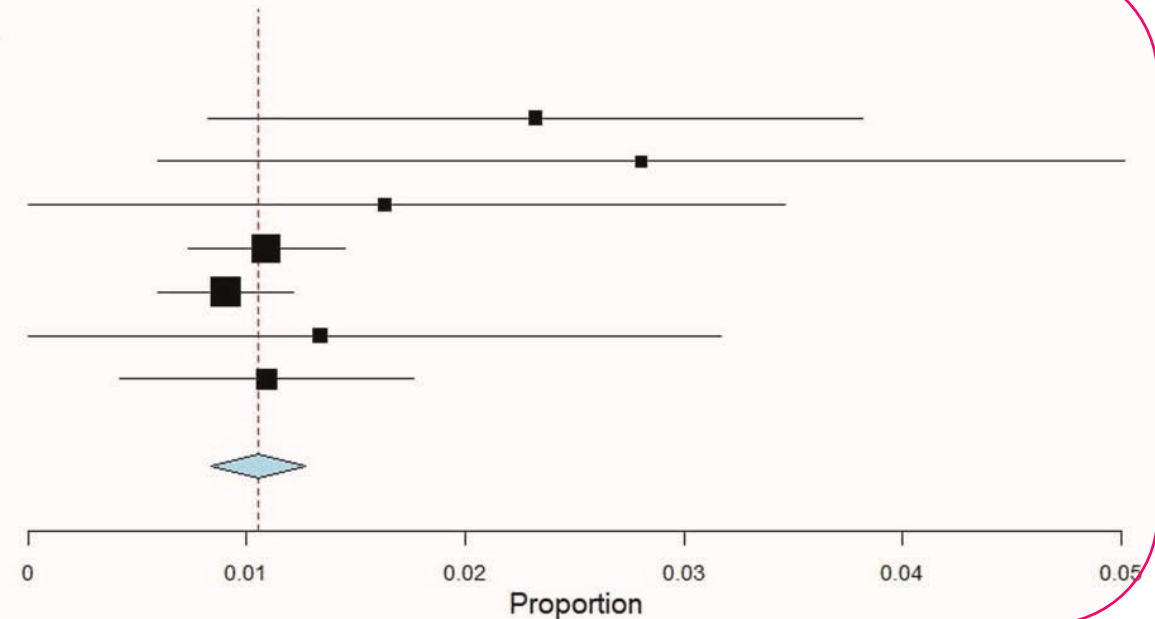


Studies	Estimate (95% C.I.)	AIS cases/ COVID-19 patients
Helms et al	0.013 (0.000, 0.032)	2/150
Klok et al	0.027 (0.004, 0.051)	5/184
Lodigiani et al	0.025 (0.009, 0.041)	9/362
Mao et al	0.023 (0.003, 0.044)	5/214
Yaghi et al	0.009 (0.006, 0.012)	32/3556
Overall ($I^2=47%$, $P=0.111$)	0.016 (0.008, 0.025)	53/4466



Tsivgoulis, Stroke July 2020

Studies	Estimate 95% (CI)	Stroke cases/COVID-19 patients
Lodgiani et al., 2020	0.023 (0.008, 0.038)	9/388
Mao et al., 2020	0.028 (0.006, 0.050)	6/214
Klok et al., 2020	0.016 (0.000, 0.035)	3/184
Jain et al., 2020	0.011 (0.007, 0.014)	35/3218
Yaghi et al., 2020	0.009 (0.006, 0.012)	32/3556
Helms et al., 2020	0.013 (0.000, 0.032)	2/150
Xiong et al., 2020	0.011 (0.004, 0.018)	10/917
Overall ($I^2=0%$, $P=0.359$)	0.011 (0.008, 0.013)	97/8627



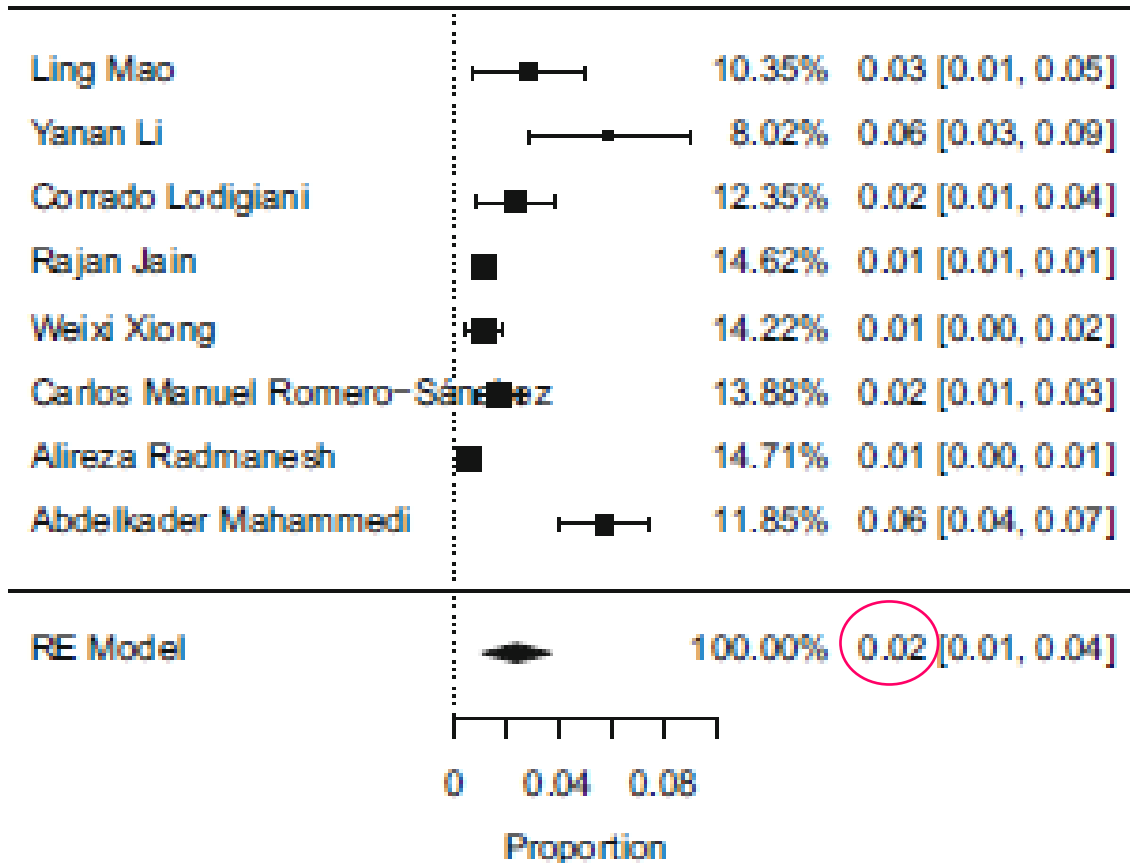
Lee et al, Front Neurol Oct 2020

Acute CVD in patients with COVID-19 0.5–5.9%

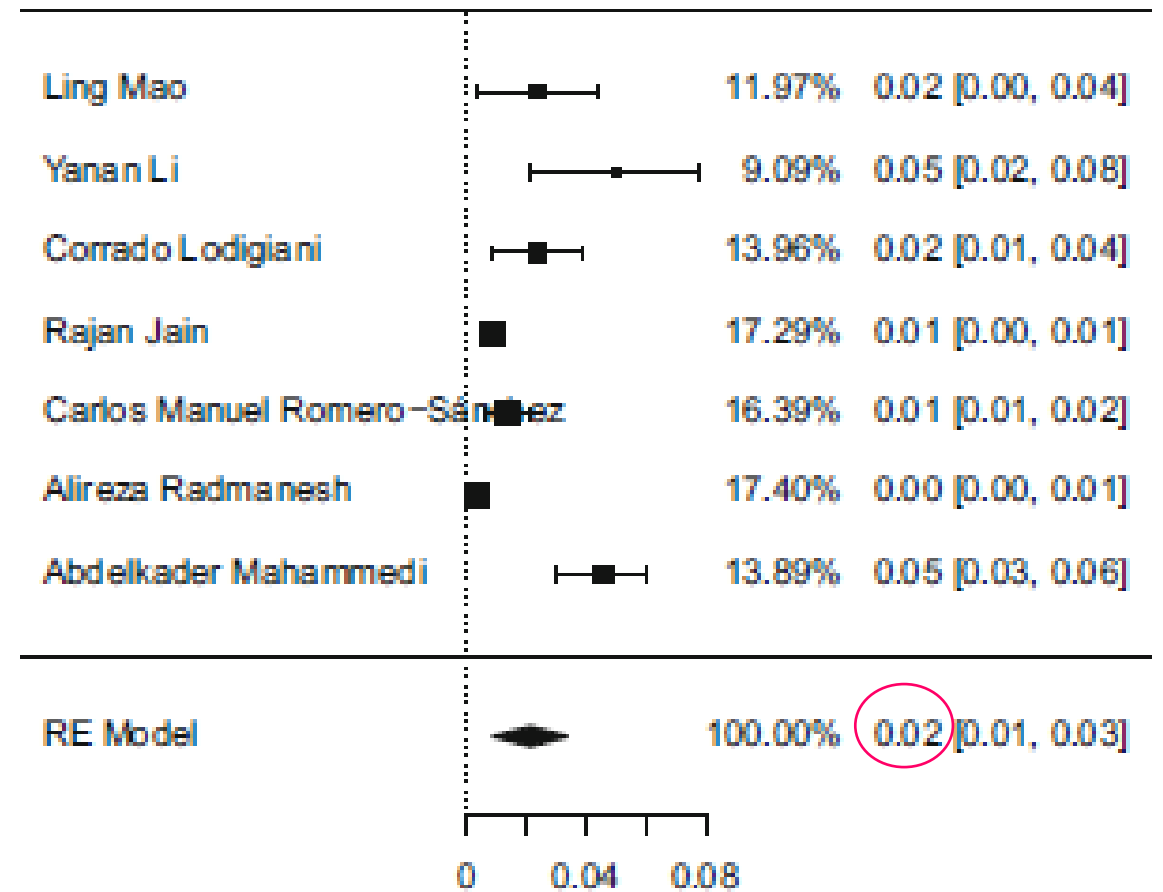
* ↑ Acute CVD in severe/ICU patients = 0.8–9.8%*

Favas *et al*, Neurological Sciences Oct 2020

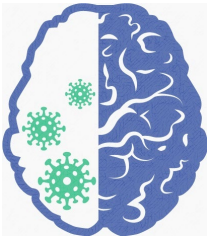
acute CVD



ischemic stroke



STROKE AND COVID-19: What we know?



Patients with a previous history of cerebrovascular disease have more severe COVID-19

↑ SEVERE COVID in patients with PREVIOUS STROKE *versus* none

↑ ARDS 32% x 19% (p .028)

↑ ICU/MV/Death 28% x 16% (p .021)

- ↑ vascular risk factors (diabetes, hypertension, vascular diseases)-

Propensity Score Matching and Adjusted (n 241)

↑ Death 14.3% x 13.0% (p .034)

↑ ICU/MV/Deaths 32.7% x 19.3% (p .037)

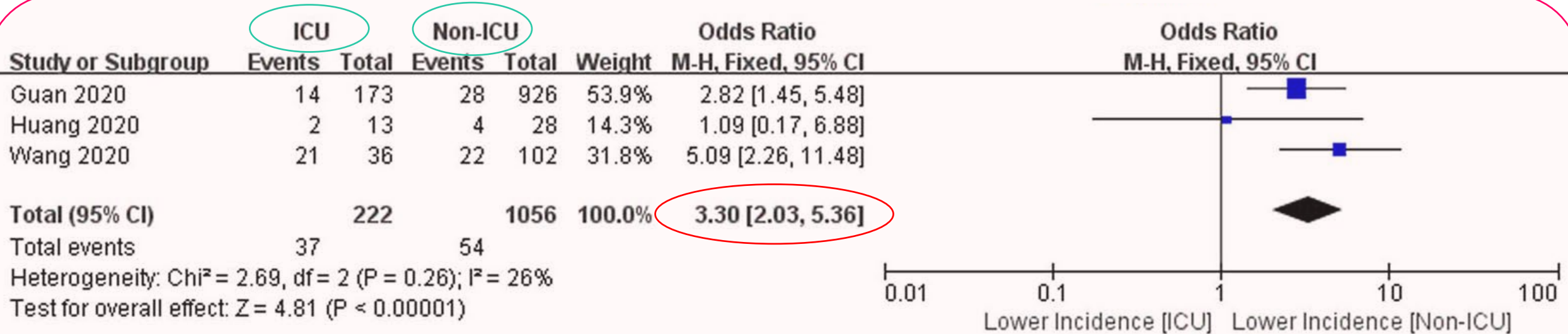
OR 1.95 (CI 1.08 - 3.52; p .026)

1,875 COVID cases in 1 centre of China (Qin *et al* Stroke)

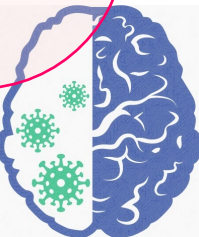
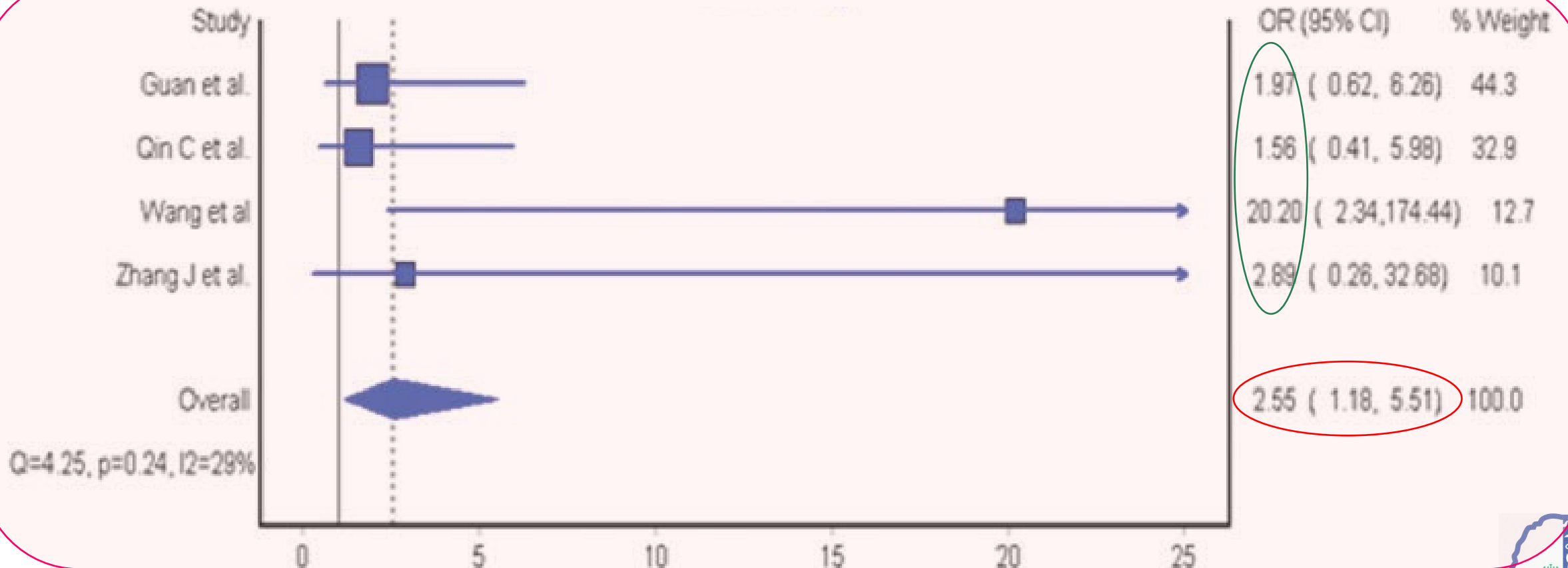


& VISE-VERSA

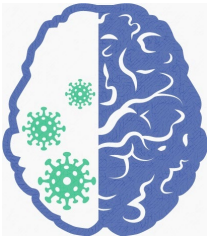
↑ CCVD in ICU COVID *versus* non-ICU → 17% vs 6%



CVD 2.5 X more frequent in severe/fatal COVID



STROKE AND COVID-19: What we know?



Patients with a concurrent acute stroke present
more severe COVID-19

↑ ACUTE STROKE in SEVERE COVID *versus* non-severe

5.7% vs 0.8% (p .03)

214 COVID cases in 3 centres of China (Mao *et al* JAMA Neurol)

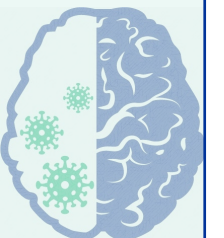
& VISE-VERSA

↑ SEVERE COVID in STROKE cases *versus* non-stroke

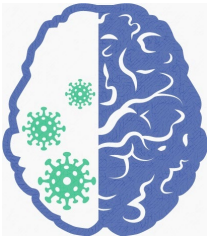
↑ **SEVERE PNEUMONIA** 80% x 40% (p .009)

- ↑ cardiovascular risk factors: 91% x 36% (p .001) -

219 COVID cases in 1 centre of China (Li *et al* Stroke Vasc Neurol)



STROKE AND COVID-19: What we know?



Stroke is more severe in patients with COVID-19

STROKE in COVID *versus* stroke non-COVID

↑ **Large Vessel Occlusion** 32% X 15% = OR 2.4 (CI 2.1–2.7; p .011)
- adjusted for cardiovascular risk factors and ethnicity -

329 patients with stroke in 6 centres of NY-USA (Kihira AJR:216, January 2021)

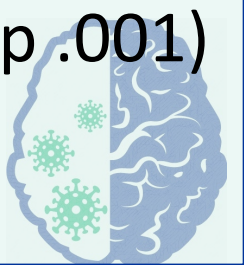
↑ **LVO** (TOAST class) 41% x 24% (p .0001)

↑ **TOTAL ANTERIOR CIRCULATION** (Bamford Class) 34% x 6% (p .0001)

↑ **CLINICAL SCORE** (NIHSS > 10) 34% x 17% (p .0001)

↑ **POOR FUNCTIONAL PROGNOSIS** (mRS 3-6 at discharge) 72% x 48% (p .001)

248 stroke cases in 1 centre of Qatar (Akhtar *et al* J Stroke Cerebrovasc Dis)



STROKE in COVID* *versus* stroke non-COVID

*swab was done if a positive clinical screening

↑ **DEATH** OR 64.87 (CI 4.44 - 987.28; p .002)

- adjusted for age and NIHSS score -

78 ischaemic stroke in a single centre of NY-USA (Yaghi *et al* Stroke)

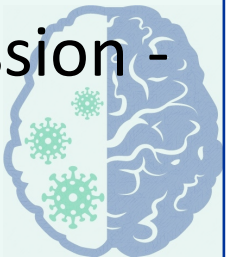
↑ **CLINICAL SCORE** (NIHSS discharge) 2 x 9 (p .005)

↑ **POOR FUNCTIONAL PROGNOSIS** (mRS discharge) 2 x 5 (p <.001)

↑ **DEATH** 35% x 6% (p < .001)

- similar distribution of cardiovascular risk factors and severity at admission -

111 critical cases of stroke in 1 ICU of Italy (Benussi *et al* Neurology)



STROKE in COVID* *versus* stroke nonCOVID

*swab was done if a positive clinical screening

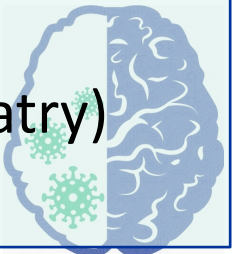
Ischaemic Stroke 94% x 86% (p .03)

- ↑ CRP and D-dimer
- ↑ DEATH 19.8% x 9.6% ($p < .000$)
- ↓ FUNCTIONAL (mRS discharge) 4 x 3 ($p < .000$)

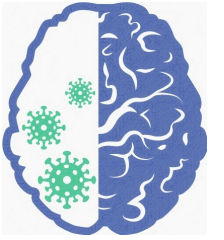
↑ **COVID at onset of FATAL STROKE OR 2.1** (1.08-4.13; $p .03$)

-adjusted for severity at admission and vascular risk factors-

1,507 stroke events in 13 hospitals of UK (Perry *et al* J Neurol Neurosurg Psychiatry)



What we still need to know?



Are the observations on stroke and COVID-19 just a concurrence due to the high force of the pandemic?

Or in fact could the SARS-CoV-2 cause stroke?

STROKE in COVID *versus* influenza admissions

1.6% x 0.2%

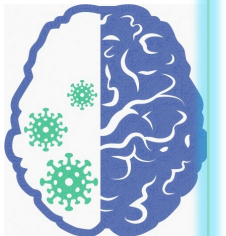
OR 4.6 (CI 1.4 - 15.7)

-adjusted for vascular risk factors and ICU admission-

1,916 COVID cohort vs 1,486 influenza historical cohort

2 centres of USA (Merkler *et al* JAMA Neurol)

What about a reverse causation or
a two-way causal relationship?



VO

ogenic

stroke

ection

A

B

C

D



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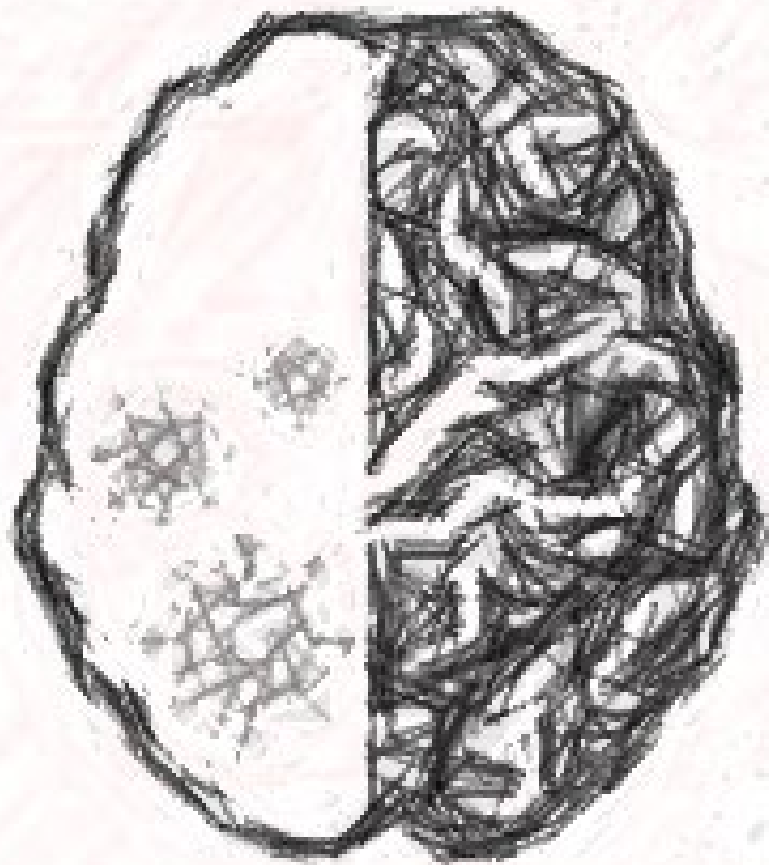
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