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
Tens of observational studies were published reporting on almost 300 acute stroke cases in patients with COVID-19.
<table>
<thead>
<tr>
<th>Country</th>
<th>IS</th>
<th>ICH</th>
<th>CVST</th>
<th>Total 297</th>
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<tr>
<td>China</td>
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<td>18</td>
<td>Mao et al (JAMA Neurol); Li et al (J Stroke Vasc Neurol); Zhang et al (NEJM)</td>
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<td>Qatar</td>
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<td>Akhtar et al (J Stroke Vasc Neurol)</td>
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<td>Iran</td>
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<td>Sharif-Razavi et al (J Neuro Sciences); Sharif-Razavi et al (NewMicrobes NewInfect); Hemasian et al (Rev Neurol)</td>
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<td>Turkey</td>
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<td>Tunç et al (J Clin Neuroscience)</td>
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<td>Dubai</td>
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<td>-</td>
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<td>Khan et al (Int J Stroke)</td>
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<td>Italy</td>
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<td>5</td>
<td>1</td>
<td>54</td>
<td>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)</td>
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<td>Spain</td>
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<td>-</td>
<td>1</td>
<td>González-Pinto et al (Eur J Neurol)</td>
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<td>France</td>
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<td>-</td>
<td>-</td>
<td>14</td>
<td>Viguier et al (J Neuroradiol); Helmes (NEJM); Escalard et al (Stroke)</td>
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<td>UK</td>
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<td>73</td>
<td>Beyrouti et al (J Neurol Neurosurg Psychiatry); Hughes et al (Eur J Case Reports Int Med); VaraTharaj et al (Lancet Psych)</td>
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<td>Netherlands</td>
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<td>-</td>
<td>-</td>
<td>3</td>
<td>Klok et al (Thrombosis Research)</td>
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<td>USA</td>
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<td>115</td>
<td>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)</td>
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<td>Brazil</td>
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<td>-</td>
<td>6</td>
<td>Lima et al (Arq Neuropsiq); Estofolete et al (J Med Virol); César-Júnior et al (Int J Stroke)</td>
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</tbody>
</table>
Strokes are been 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 haemorragic cases
Time between COVID and neurologic symptoms = 9.5 days (0-33)
19% of cases died
### Studies: AIS cases/COVID-19 patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Estimate (95% C.I.)</th>
<th>Proportion</th>
<th>N/Total</th>
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<tbody>
<tr>
<td>Helms et al, 2020</td>
<td>0.013 (0.000, 0.032)</td>
<td>2/150</td>
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<tr>
<td>Klok et al, 2020</td>
<td>0.027 (0.004, 0.051)</td>
<td>5/184</td>
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<tr>
<td>Lodigiani et al, 2020</td>
<td>0.025 (0.009, 0.041)</td>
<td>9/362</td>
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<tr>
<td>Mao et al, 2020</td>
<td>0.023 (0.003, 0.044)</td>
<td>5/214</td>
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<tr>
<td>Yaghi et al, 2020</td>
<td>0.009 (0.006, 0.012)</td>
<td>32/3556</td>
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<tr>
<td><strong>Overall (I²=47%, P=0.111)</strong></td>
<td><strong>0.016 (0.008, 0.025)</strong></td>
<td><strong>53/4466</strong></td>
<td></td>
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</tbody>
</table>

Tsivgoulis, Stroke July 2020

### Studies: Stroke cases/COVID-19 patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Estimate 95% (CI)</th>
<th>Proportion</th>
<th>N/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lodigiani et al, 2020</td>
<td>0.023 (0.008, 0.038)</td>
<td>9/388</td>
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<tr>
<td>Mao et al, 2020</td>
<td>0.028 (0.006, 0.050)</td>
<td>6/214</td>
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<tr>
<td>Klok et al, 2020</td>
<td>0.016 (0.000, 0.035)</td>
<td>3/184</td>
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<tr>
<td>Jain et al, 2020</td>
<td>0.011 (0.007, 0.014)</td>
<td>35/3218</td>
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<tr>
<td>Yaghi et al, 2020</td>
<td>0.009 (0.006, 0.012)</td>
<td>32/3556</td>
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<tr>
<td>Helms et al, 2020</td>
<td>0.013 (0.000, 0.032)</td>
<td>2/150</td>
<td></td>
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<tr>
<td>Xiong et al, 2020</td>
<td>0.011 (0.004, 0.018)</td>
<td>10/917</td>
<td></td>
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<tr>
<td><strong>Overall (I²=0%, P=0.359)</strong></td>
<td><strong>0.011 (0.008, 0.013)</strong></td>
<td><strong>97/8627</strong></td>
<td></td>
</tr>
</tbody>
</table>

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
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%

Li et al Clinical Research in Cardiology
CVD 2.5 X more frequent in severe/fatal COVID

Aggarwal et al Int J Stroke
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 Oclusion 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?
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**Principal Centre:** Fiocruz - Pernambuco  
**Funder:** INOVA PROGRAMME Fiocruz- Brazil)

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