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Morning Brief: Scientific Review

27 May 2020

The purpose of the Morning Brief is to summarize and present key information, research articles and other relevant publications pertaining to critical care and COVID-19.

Stellenbosch University Research Response Team

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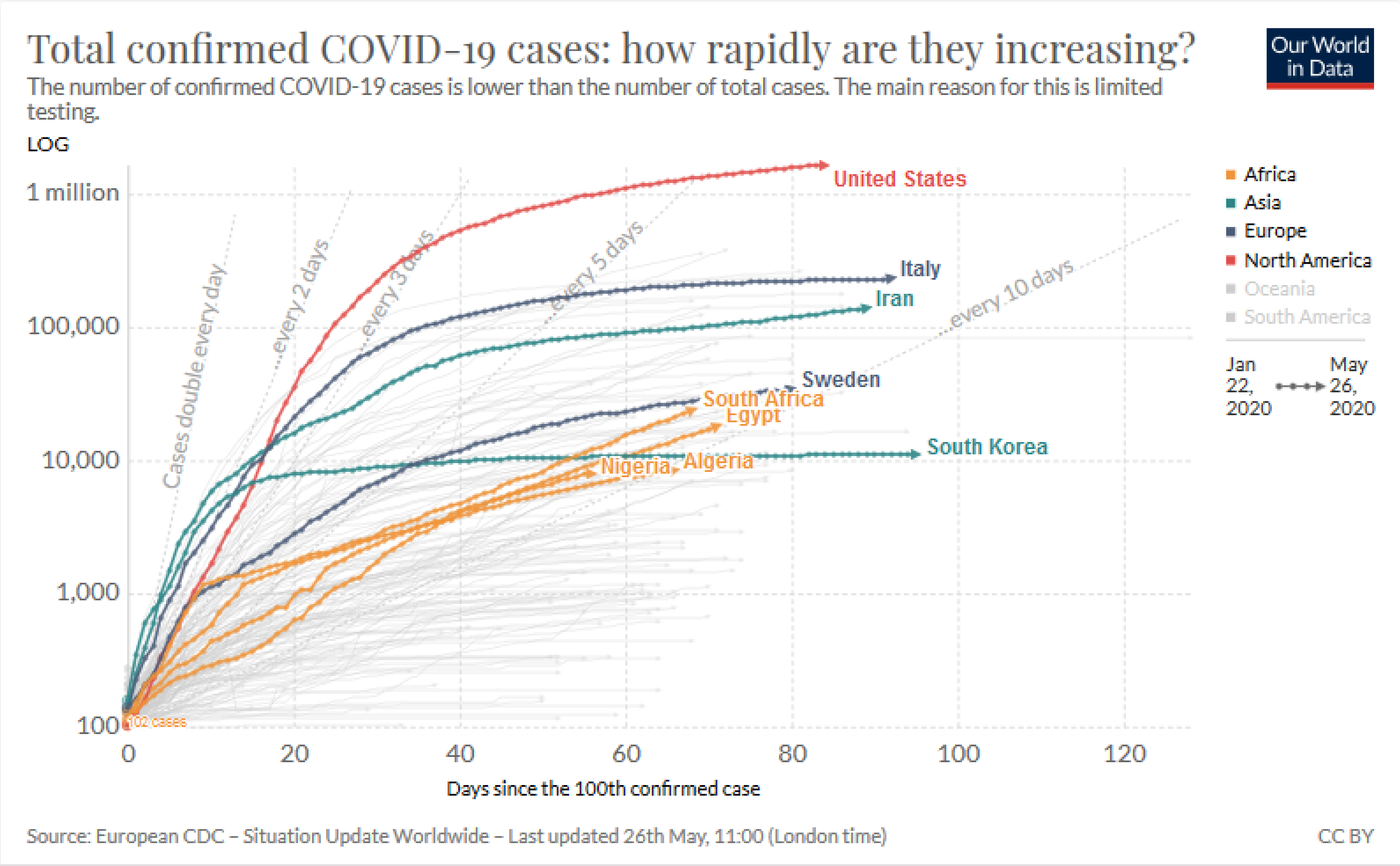
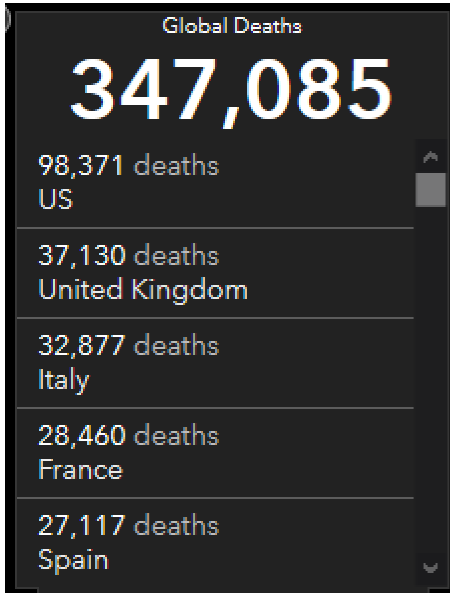
Content of the brief

- Global Statistics
- South African Statistics
- Topics:
    - Brief reports

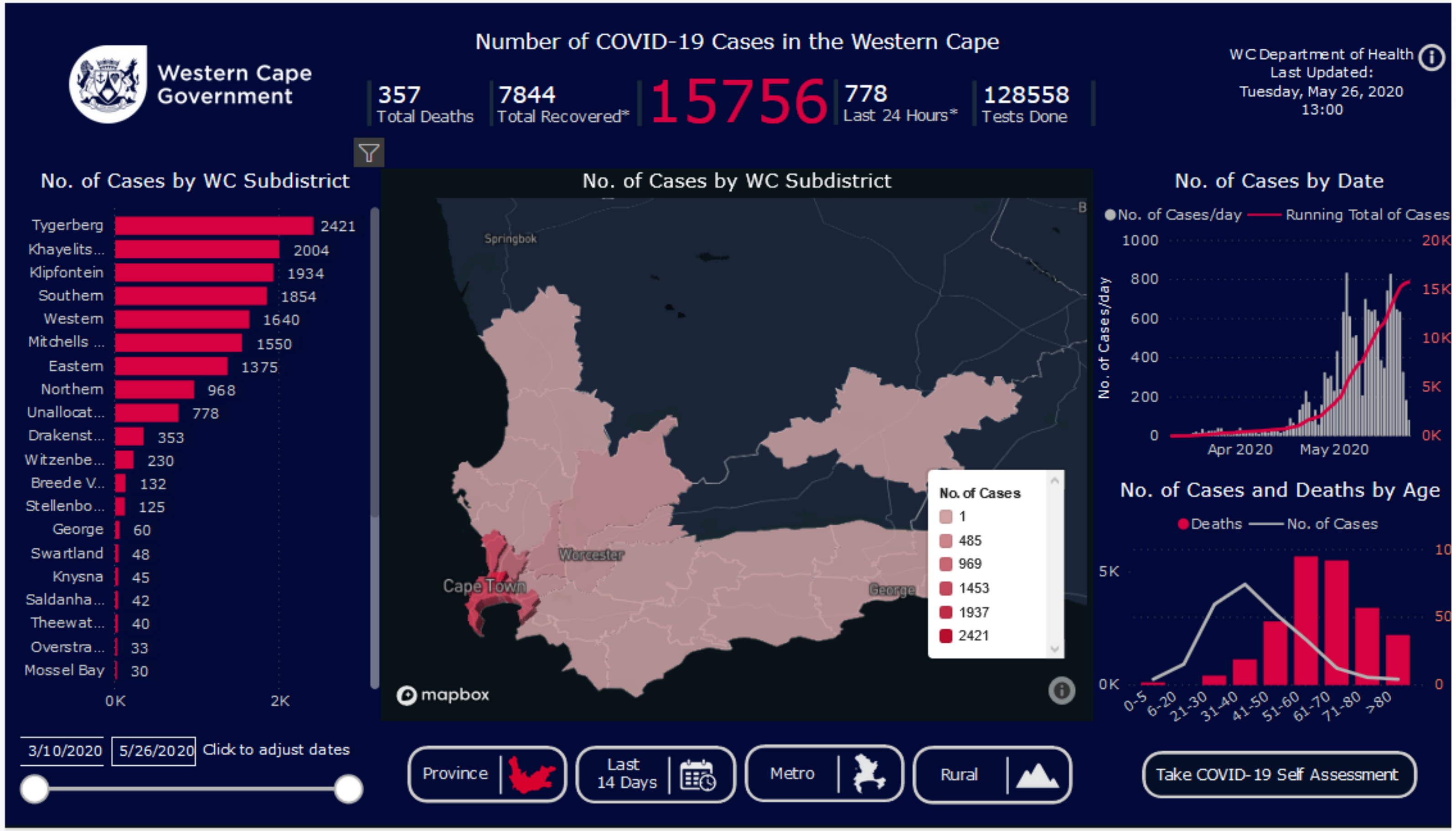
Global Statistics





Source: https://coronavirus.jhu.edu/map.html

South African Statistics



Sources: https://sacoronavirus.co.za

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Articles of Interest

The NEW ENGLAND JOURNAL of MEDICINE

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Randomised, double-blind placebo controlled trial, 60 centres, 10 countries

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

Intervention:

Remdesivir IVI, 200mg loading dose on day 1, 100mg maintenance dose daily days 2 to 10 or until hospital discharge or death

Control: placebo

Concomittant treatment: allowed if written hospital protocol, otherwise prohibited for 29 days of study follow-up.

Outcomes:

- time to recovery, with stratification by disease severity

  “recovery” defined on a pre-specified ordinal scale of clinical condition
- Mortality at day 14 and 28
- Adverse events

Results of interim analysis after enrolment complete, follow-up ongoing, data and safety monitoring board recommended unblinding of treating clinicians who could switch patients on placebo to remdesivir if clinically indicated.

Results

1063 underwent randomization; 541 remdesivir, 522 placebo

36 in each group stopped remdesivir or placebo before day 10 for adverse events

Complete follow-up for 391 remdesivir and 340 placebo patients

538 and 521 included in analysis

About 60% male in both groups, Mean age of all 58, 80% North American

Median time from symptom onset to randomisation 9 days

52% had 2 or more co-existing conditions

About 50% hypertension, 37% obesity, 30% diabetes

25% met most severe category on ordinal scale below death

See next slide

Beigel, et al. Remdesivir for the Treatment of Covid-19 — Preliminary Report, NEJM, May 22, 2020, DOI: 10.1056/NEJMoa2007764

Results continued

Time to recovery remdesivir 11 days vs 15 days placebo

Rate ratio for recovery, 1.32; 95%[CI], 1.12 to 1.55; P<0.001; 1059 patients

Adjusted for baseline severity score: 1.31; 95% CI, 1.12 to 1.54; 1017 patients

Those on mechanical ventilation or ECMO at enrolment, 272 patients rate ratio for recovery was 0.95 (95% CI, 0.64 to 1.42)

Day 14 mortality was numerically lower in the remdesivir group than in the placebo group, but the difference was not significant (hazard ratio for death, 0.70; 95% CI, 0.47 to 1.04; 1059 patients) - 32/538 (5%) vs 54/521 (10%)

Kaplan–Meier estimates of mortality by 14 days were 7.1% and 11.9%

Serious adverse events 21% vs 27%

Discussion

Only about 30% of patients in the most severe baseline category before death recovered by day 29 of study follow up – follow up may have been too short

Awaiting results of final follow-up data of whole cohort

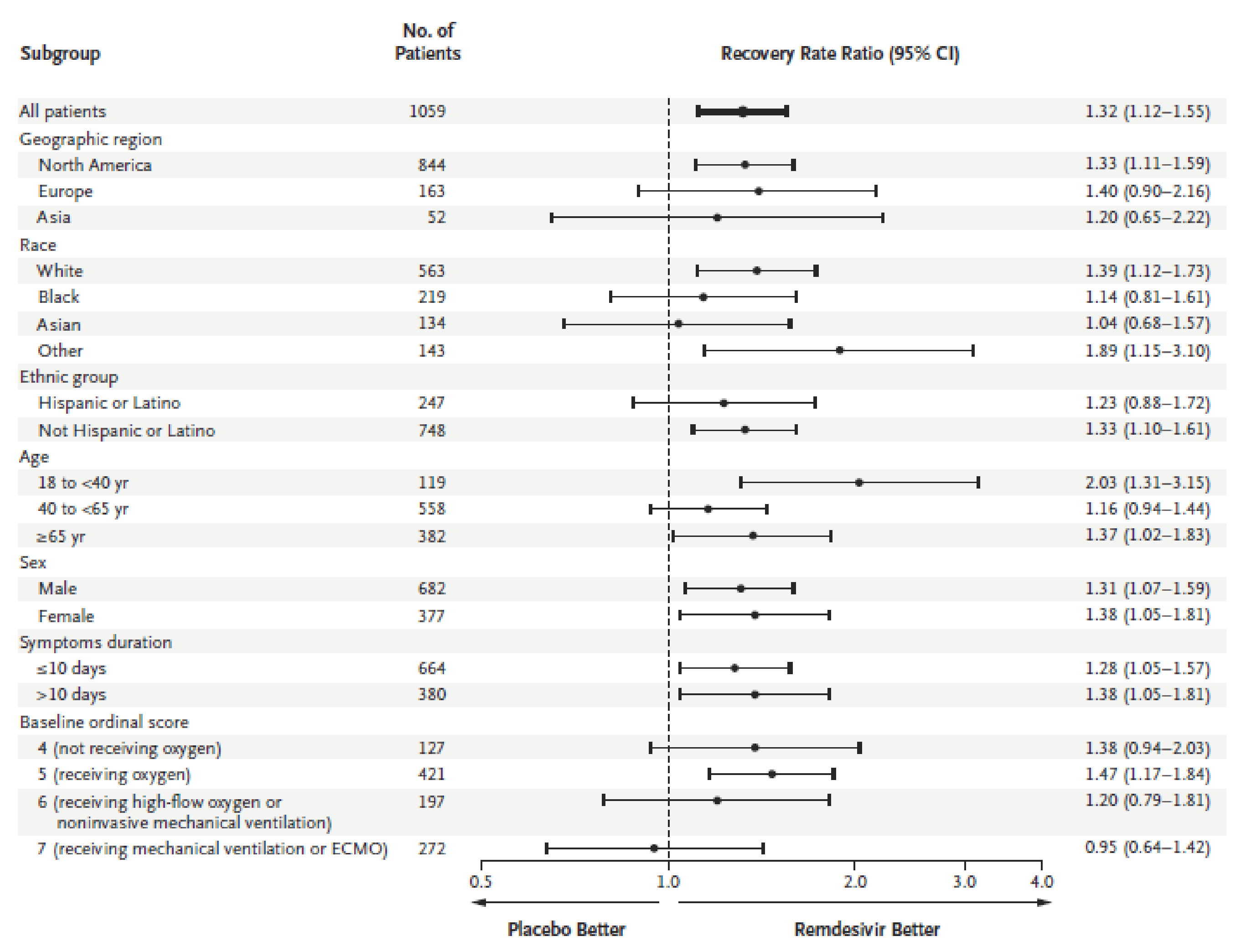

Figure 3. **Time to Recovery According to Subgroup.**
The widths of the confidence intervals have not been adjusted for multiplicity and therefore cannot be used to infer treatment effects. Race and ethnic group were reported by the patients.

Beigel, et al. Remdesivir for the Treatment of Covid-19 — Preliminary Report, NEJM, May 22, 2020, DOI: 10.1056/NEJMoa2007764

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Retrospective record review

DIABETES RESEARCH AND CLINICAL PRACTICE 164 (2020) 108214

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

ELSEVIER

International Diabetes Federation

Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients

Zhenzhou Wang [1], Zhe Du [1], Fengxue Zhu *

Trauma Center, National Center for Trauma Medicine, Key Laboratory of Trauma and Neural Regeneration, Peking University People's Hospital, Beijing 100044, China

Wuhan, China, n = 132, median age 66y, 51% male, other comorbidities – any (66%), hypertension (50%), cardiovascular disease (16%)

Divided into 3 groups by HbA1C and diabetic status:

- HbA1c level < 6.0 (n = 41)
- 2019 WHO diabetes criteria not met and HbA1c level > 6.0 (n = 44)
- Diabetes criteria met (n = 47, 66% known type 2, 34% new diagnosis)

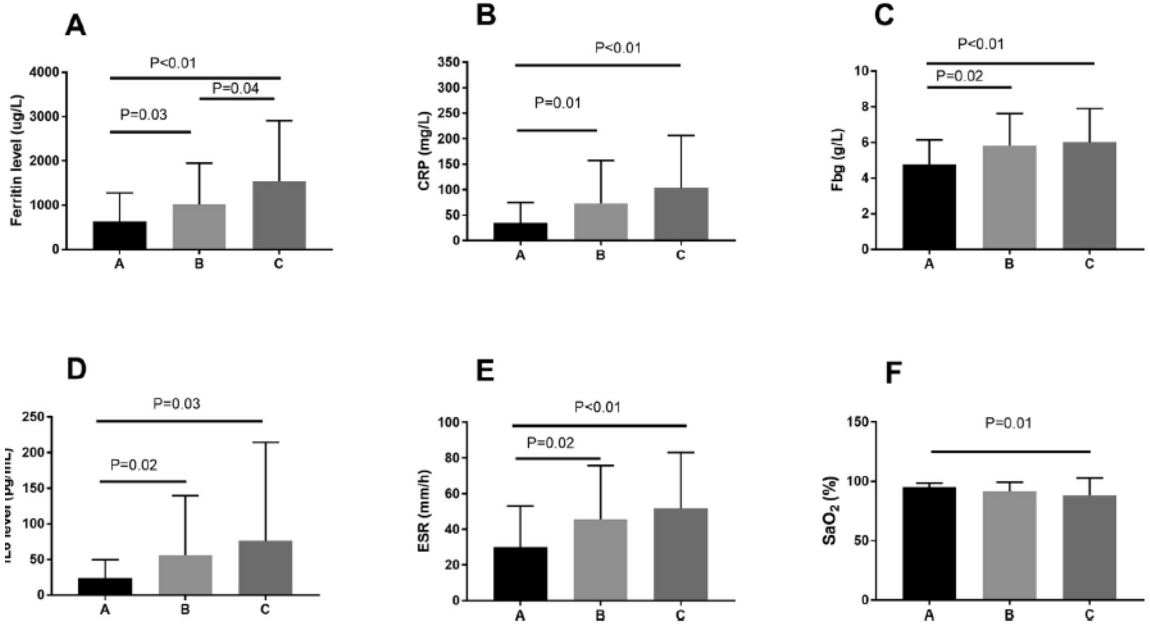


Fig. 1 – Inflammatory factors in blood and oxygen saturation among the three groups.

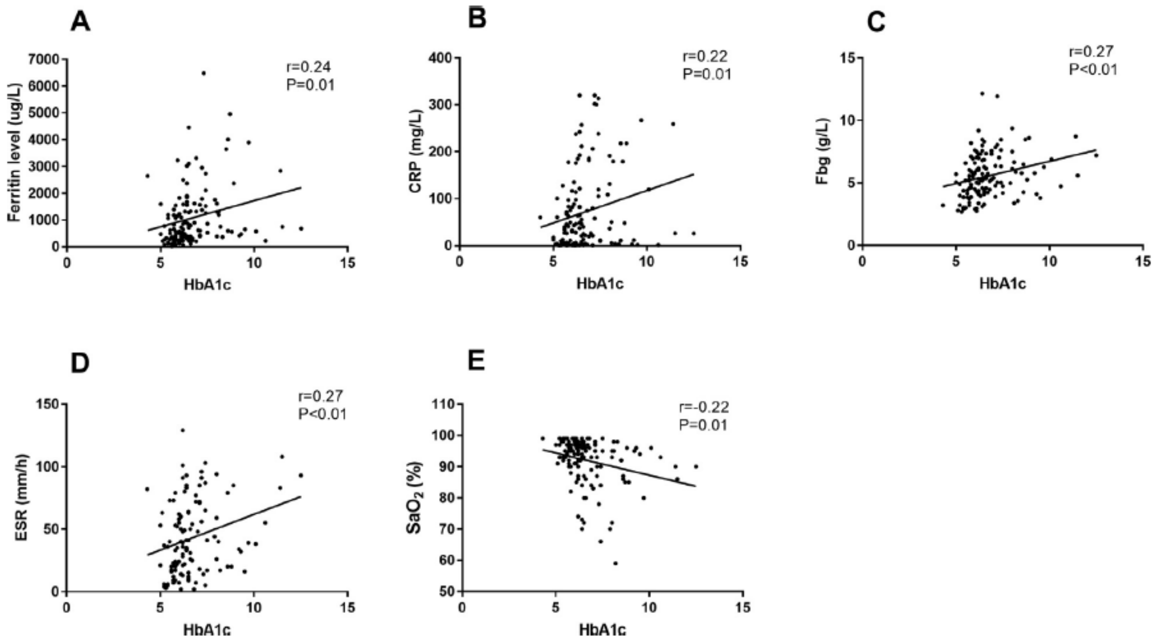
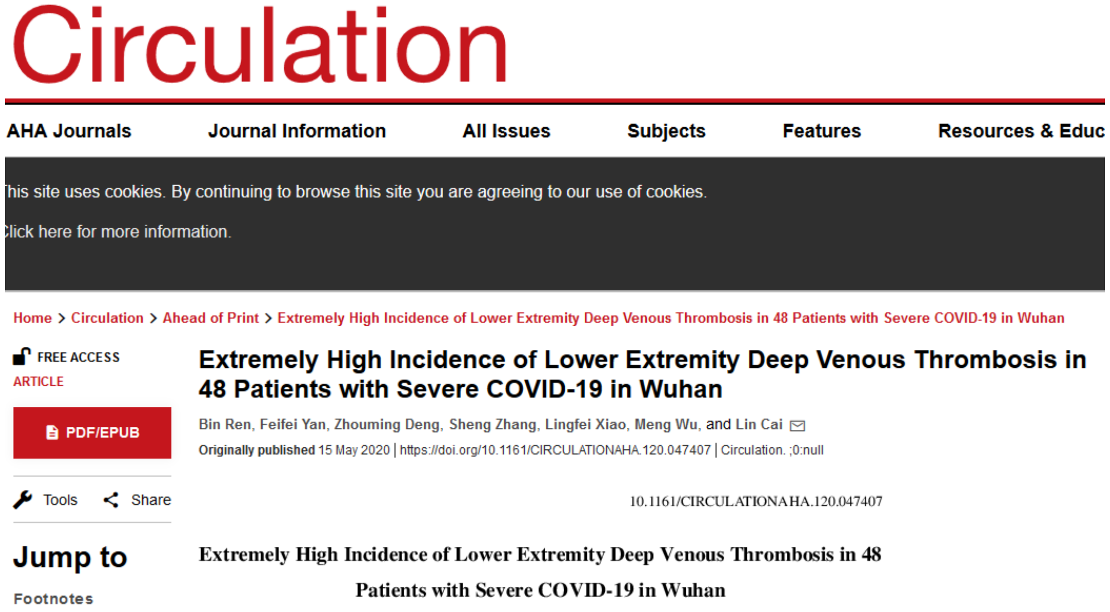


Fig. 2 – Correlation analysis of inflammatory factors, blood oxygen saturation, and HbA1c level.

Wang, Z et al. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients, Diabetes research and clinical practice 164 (2020)108214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Extremely High Incidence of Lower Extremity Deep Venous Thrombosis in 48 Patients with Severe COVID-19 in Wuhan

Bin Ren, Feifei Yan, Zhouming Deng, Sheng Zhang, Lingfei Xiao, Meng Wu, and Lin Cai

Originally published 15 May 2020 | https://doi.org/10.1161/CIRCULATIONAHA.120.047407 | Circulation. ;0:null

10.1161/CIRCULATIONAHA.120.047407

Extremely High Incidence of Lower Extremity Deep Venous Thrombosis in 48 Patients with Severe COVID-19 in Wuhan

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Wuhan, 2 hospitals, n = 48, ICU patients, median age 70 y (IQR 62 – 80), hypertension 40%, diabetes 27%, cardiovascular disease 23%

Aimed to determine prevalence of DVT by compression ultrasound examination of deep veins from inguinal ligament to the ankle

They do not describe the detailed procedure or comment on the accuracy of the selected method to diagnose DVT in a screening situation.

47/48 on prophylactic LMWH

29 mechanical ventilation, 18 endotracheal intubation

Lower extremity DVT detected in 41/48 patients (85%)

- 36 distal
- 5 proximal

median level of D-dimer in

- no DVT 0.90 (0.51-3.10),
- isolated distal DVT 5.31 (1.12-9.78)
- proximal DVT 3.53 (1.87-11.64) (P=0.09)

Difference in mortality proportion not significant (28%, 27%, 60%)

Cross-sectional study

Discussion

Cite a critical care RCT prevalence of DVT of 6% and an H1N1 study with DVT prevalence 13%, but they don't comment on the ages of participants in those studies.

Limitations

No follow up reporting apart from mortality

Bin Ren et al., Extremely High Incidence of Lower Extremity Deep Venous Thrombosis in 48 Patients with Severe COVID-19 in Wuhan, 15 May 2020 https://doi.org/10.1161/CIRCULATIONAHA.120.047407Circulation

This summary was prepared by Dr E Maasdorp as part of the daily brief to the TBH ICU team.