



新型冠状病毒信息 简报

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上海科技大学免疫化学研究所

生物学大数据平台和高通量筛选平台领衔编译制作

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免责声明：

本简报仅作为科研参考之用，不构成医疗建议，如您怀疑自己感染新型冠状病毒，请去正规医院或者咨询医生。

1. 2020年5月13日疫情

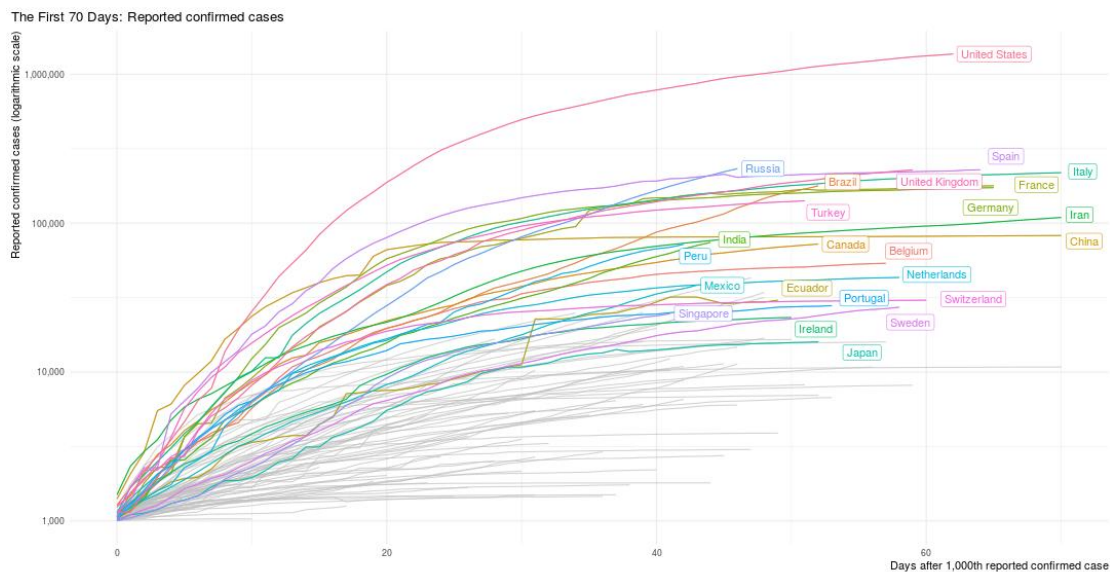
数据来源：WHO

发布时间：2020年4月25日北京时间下午4点

链接：<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>

根据 WHO 提供的数据，2020年5月13日全球累计确诊新型冠状病毒病人 4170424 例，当日新增确诊 81577 例，累计死亡 287399 例，当日新增死亡 4245。

中国累计确诊 84458 例，累计死亡 4644 例，当日新增确诊 7 例，新增死亡 0 例。



Case data: Johns Hopkins University Center for Systems Science and Engineering (JHU CSSE). Data obtained on May 13, 2020. The sample is limited to countries with at least 7 days of data. Code: <https://github.com/joachim-gassen/tidycovid19>.

重点国家确诊数量曲线（<https://jgassen.shinyapps.io/tidycovid19/>，数据截止5月13日北京时间下午4点）



全国新型冠状病毒肺炎新增确诊病例分布图（5月13日，来源：

<http://2019ncov.chinacdc.cn/2019-nCoV/>）

2. SARS-CoV-2 RNA 复阳的临床病程和危险因素：一项来自中国武汉的回顾性队列研究
Clinical Course and Risk Factors for Recurrence of Positive SARS-CoV-2 RNA: A Retrospective Cohort Study from Wuhan, China

来源: medRxiv

发布时间: 2020-05-12

链接: <https://www.medrxiv.org/content/10.1101/2020.05.08.20095018v1>

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中文摘要:

背景: 2019 冠状病毒病 (COVID-19) 由严重急性呼吸系统综合征冠状病毒 2 型 (SARS-CoV-2) 引起, 现已发展为全球性大流行。据报道, 符合医院出院标准的 COVID-19 患者 (包括连续 2 次 RT-PCR 阴性结果) 出现了 PCR 复阳性。然而, 这些患者的临床病程和危险因素尚未得到很好的描述。

方法: 采用回顾性队列研究方法, 选取 2020 年 2 月 24 日至 2020 年 3 月 31 日湖北省妇幼保健院光谷院区经 RT-PCR 确诊的 2019 冠状病毒病患者。从病历中提取流行病学、放射学、实验室、治疗和结局数据。采用单变量和多变量逻辑回归方法来阐明患者 SARS-CoV-2 RNA 复阳的危险因素。

结果: 本研究纳入 1087 例 COVID-19 患者, 其中 20 人 (1.8%) 死亡, 1067 人 (98.2%) 出院。在出院的病例中, 有 81 例 (7.6%) 患者出现了 SARS-CoV-2 RNA 复阳结果。年龄大显然与死亡相关。对于 RT-PCR 复阳性患者, 从发病至完全 RNA 阴性的中位病程为 33.0 天 (范围为 6.0-82.0 天; IQR: 20.0-41.0 天), 而从发病到复发为 50.0 天 (范围为 21.0-95.0 天; IQR: 36.5-59.5 天)。多因素回归分析发现, SARS-CoV-2 RNA 复阳与住院期间 IL-6 水平升高 ($P=0.004$, $OR=3.050$; 95% CI, 1.432-6.499), 淋巴细胞计数增加 ($P=0.038$, $OR=2.321$; 95% CI, 1.048-5.138) 及肺实变的 CT 影像学特征 ($P=0.038$, $OR=1.641$; 95% CI, 1.028-2.620) 有关。

结论: 外周血淋巴细胞计数、IL-6 水平的升高以及 CT 影像的实变特征是临床医生识别有 SARS-CoV-2 RNA 复阳性风险的患者的的重要危险因素。据推测, 这可能是在对抗病毒毒性时, 免疫调节的平衡造成的。对于复阳性风险高的患者, 应在发病后至少 50 天内进行长期观察并采取额外的预防措施, 以预防未来的暴发。

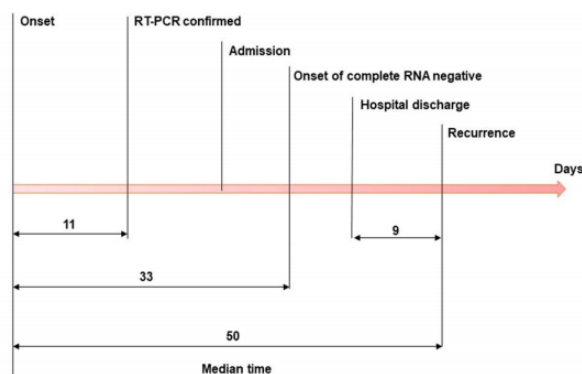


Figure 2. The median duration of different stages in patients with recurrence of positive SARS-CoV-2 RNA after discharge. Figure shows the median duration from

illness onset to initial RT-PCR confirmed, onset of complete RNA negative and recurrent RT-PCR positivity after discharge, and from discharge to recurrence.

Abstract:

Background: Coronavirus Disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has developed into a full-blown global pandemic. It has been reported that patients with COVID-19 meeting the criteria for hospital discharge (including two consecutive negative RT-PCR results) have experienced recurrent PCR positivity. However, the clinical course and risk factors for these patients have not been well described.

Methods: In this retrospective cohort study, consecutive patients with COVID-19 confirmed by RT-PCR from the Guanggu Branch of Hubei Province Maternity and Childcare Hospital from February 24, 2020 to March 31, 2020 were enrolled. The epidemiological, radiographic, laboratory, treatment, and outcome data were extracted from medical records. Univariate and multivariable logistic regression methods were used to elucidate risk factors for patients with recurrence of positive SARS-CoV-2 RNA.

Results: 1087 COVID-19 patients were included in this study. Of these, 20 (1.8%) died and 1067 (98.2%) were discharged from the hospital. Among the discharged cases, there were 81 (7.6%) patients found to develop a repeat positive SARS-CoV-2 RNA result. Older age was obviously associated with death. For patients with recurrent RT-PCR positivity, the median duration from illness onset to onset of complete RNA negative was 33.0 days (range, 6.0–82.0 days; IQR, 20.0–41.0 days), while that from illness onset to recurrence was 50.0 days (range, 21.0–95.0 days; IQR, 36.5–59.5 days). Multivariate regression analysis identified recurrence of positive SARS-CoV-2 RNA was associated with elevated IL-6 levels ($P=0.004$, $OR=3.050$; 95% CI, 1.432–6.499), increased lymphocyte count ($P=0.038$, $OR=2.321$; 95% CI, 1.048–5.138) and CT imaging features of lung consolidation ($P=0.038$, $OR=1.641$; 95% CI, 1.028–2.620) during hospitalization.

Conclusion: Elevated lymphocyte counts and IL-6 levels in blood, and consolidation features on CT imaging are useful risk factors for clinicians to identify patients at risk of developing recurrent positivity of SARS-CoV-2 RNA. This is speculated to be caused by a balance in immune regulation when fighting virus toxicity. For patients with a high risk of recurrent positivity, a prolonged observation and additional preventative measures should be implemented for at least 50 days after illness onset to prevent future outbreaks.

3. 美国和加拿大小儿重症监护病房收治的儿童冠状病毒病 2019 (COVID-19) 感染的特征和结果

Characteristics and Outcomes of Children with Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units

来源: JAMA

发布时间: 2020-05-11

链接: <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2766037>

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DOI 或 PUBMED ID: 10.1001/jamapediatrics.2020.1948

编译者: 张鹏伟

中文摘要:

重要性: 最近和正在进行的 2019 年冠状病毒病 (COVID-19) 大流行对患有 COVID-19 感染的成人重症患者造成了前所未有的损失。虽然有证据表明住院儿童的 COVID-19 感染负担比成人轻, 但迄今为止, 在儿科重症监护病房 (PICUs) 中描述 COVID-19 的报道有限。

目的: 提供北美 PICUs 中 COVID-19 感染的早期描述和特征, 着重于表现方式、合并症的存在、疾病的严重程度、治疗干预、临床轨迹和早期结果。

设计、设置和参与者: 这项横断面研究包括了在 2020 年 3 月 14 日至 4 月 3 日期间, 46 名北美 PICUs 的 COVID-19 阳性儿童。后续至 2020 年 4 月 10 日。

主要成果和措施: PICUs 确诊 COVID-19 感染患儿的院前特点、临床轨迹和住院结果。

结果: 在参与 PICUs 的 48 名 COVID-19 患儿中, 25 名 (52%) 为男孩, 中位 (范围) 年龄为 13 岁 (4.2-16.6)。40 名患者 (83%) 有明显的既往共病; 35 名 (73%) 有呼吸症状, 18 名 (38%) 需要有创通气。11 例 (23%) 有 2 个或多个器官系统衰竭。1 例 (2%) 需要体外膜肺氧合。靶向疗法用于 28 例患者 (61%), 其中羟氯喹是最常用的药物, 无论是单独使用 (11 名患者) 还是联合使用 (10 例患者)。在随访期结束时, 有 2 例患者 (4%) 死亡, 仍有 15 例 (31%) 住院, 其中 3 例仍需要通气支持, 1 例接受了体外膜氧合。出院者的 PICU 中位数 (范围) 和住院天数分别为 5 (3-9) 天和 7 (4-13) 天。

结论与相关性: 这份早期报告描述了北美 PICU 中 COVID-19 感染的负担, 并证实儿童严重疾病的发生率很高, 但远不及成年人。院前合并症似乎是儿童的一个重要因素。这些初步观察为更大更广泛的 COVID-19 感染儿童研究提供了重要平台。

Abstract:

Importance: The recent and ongoing coronavirus disease 2019 (COVID-19) pandemic has taken an unprecedented toll on adults critically ill with COVID-19 infection. While there is evidence that the burden of COVID-19 infection in hospitalized children is lesser than in their adult counterparts, to date, there are only limited reports describing COVID-19 in pediatric intensive care units (PICUs).

Objective: To provide an early description and characterization of COVID-19 infection in North American PICUs, focusing on mode of presentation, presence of comorbidities, severity of disease, therapeutic interventions, clinical trajectory, and early outcomes.

Design, Setting, and Participants: This cross-sectional study included children positive for COVID-19 admitted to 46 North American PICUs between March 14 and April 3, 2020, with follow-up to April 10, 2020.

Main Outcomes and Measures: Prehospital characteristics, clinical trajectory, and hospital outcomes of children admitted to PICUs with confirmed COVID-19 infection.

Results: Of the 48 children with COVID-19 admitted to participating PICUs, 25 (52%) were male, and the median (range) age was 13 (4.2-16.6) years. Forty

patients (83%) had significant preexisting comorbidities; 35 (73%) presented with respiratory symptoms and 18 (38%) required invasive ventilation. Eleven patients (23%) had failure of 2 or more organ systems. Extracorporeal membrane oxygenation was required for 1 patient (2%). Targeted therapies were used in 28 patients (61%), with hydroxychloroquine being the most commonly used agent either alone (11 patients) or in combination (10 patients). At the completion of the follow-up period, 2 patients (4%) had died and 15 (31%) were still hospitalized, with 3 still requiring ventilatory support and 1 receiving extracorporeal membrane oxygenation. The median (range) PICU and hospital lengths of stay for those who had been discharged were 5 (3-9) days and 7 (4-13) days, respectively.

Conclusions and Relevance: This early report describes the burden of COVID-19 infection in North American PICUs and confirms that severe illness in children is significant but far less frequent than in adults. Prehospital comorbidities appear to be an important factor in children. These preliminary observations provide an important platform for larger and more extensive studies of children with COVID-19 infection.

4. COVID-19 患者的视网膜表现

Retinal findings in patients with COVID-19

来源: The Lancet Journal

发布时间: 2020-05-12

链接: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31014-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31014-X/fulltext)

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DOI 或 PUBMED ID: [https://doi.org/10.1016/S0140-6736\(20\)31014-X](https://doi.org/10.1016/S0140-6736(20)31014-X)

编译者: 王玮

中文摘要:

COVID-19 已被证明影响身体不同部位, 包括眼部疾病如结膜炎。

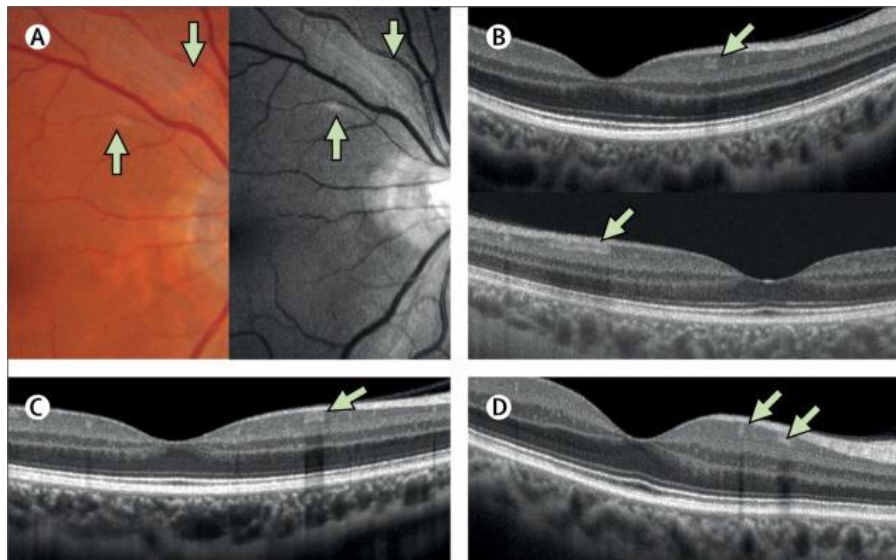
光学相干层析成像 (OCT) 是一种非侵入式成像技术, 可用于显示糖尿病, 帕金森病, 阿尔茨海默病等全身疾病以及许多病毒感染引起的亚临床视网膜改变。该研究使用 OCT 来评估 SARS-CoV-2 感染患者。该协议得到了相关伦理委员会的批准。

该研究报告了 12 名成人 (6 男 6 女, 年龄 25-69 岁) 在 COVID-19 症状出现后 11-33 天的视网膜和 OCT 变化。所有患者均有发热、乏力和呼吸困难, 11 例患者同时出现嗅觉缺失。两名病人入院治疗, 但无一人需要重症监护。9 名病人是内科医生, 2 名是医护人员。所有患者在眼科检查时血液参数正常。9 名患者经 PCR (鼻腔和口腔拭子) 检测 SARS-CoV-2 阳性, 2 名患者经 COVID-19 抗体检测阳性。使用了两种不同的 OCT 设备: DRI-OCT Triton Swept Source (Topcon, Tokyo, Japan) 和 XR Avanti SD-OCT (Optovue, Fremont, CA, USA)。

所有患者均表现为神经节细胞水平的高反射性病变, 双眼视乳头黄斑束内丛状层的高反射性病变更为明显 (图一)。OCT 血管造影及神经节细胞复合物分析结果正常。此外, 4 名患者

在眼底检查、彩色眼底摄影和无红成像中观察到沿视网膜拱廊有细微的棉絮斑和微出血。所有患者的视力和瞳孔反射正常，没有发现眼内炎症的症状或体征。

尽管动物模型显示眼部病变可能包括视网膜炎和视神经炎，但据我们所知，这是首次报道可能与人类 COVID-19 感染有关的视网膜病变。神经节细胞和丛状层的发现可能与动物研究和 COVID-19 中描述的中枢神经系统表现有关事件。



图一

Abstract:

Coronavirus disease 2019 (COVID-19) has been shown to affect different parts of the body, and ophthalmological changes have been associated with ocular external diseases such as conjunctivitis.

Optical coherence tomography (OCT) is a non-invasive imaging technique that is useful for demonstrating subclinical retinal changes in systemic conditions such as diabetes, Parkinson's disease, and Alzheimer's disease, as well as many viral infections. We used OCT to evaluate patients infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The protocol was approved by INVIRARE Pesquisa Clínica Auditoria e Consultoria Institutional Review Board Ethics Committee.

Here we report retinal and OCT changes in 12 adults (six men and six women, aged 25 - 69 years), examined 11 - 33 days after COVID-19 symptom onset. All patients had fever, asthenia, and dyspnoea, and 11 patients also presented with anosmia. Two patients were admitted to hospital but none required intensive care. Nine patients were physicians, and two were health-care workers. All patients had normal blood parameters at the time of ophthalmological evaluation. Nine patients tested positive for SARS-CoV-2 by PCR (using nasal and oral swabs), and two patients tested positive in antibody tests for COVID-19. Two different OCT devices were used: DRI-OCT Triton Swept Source (Topcon, Tokyo, Japan) and XR Avanti SD-OCT (Optovue, Fremont, CA, USA).

All patients showed hyper-reflective lesions at the level of ganglion cell and inner plexiform layers more prominently at the papillomacular bundle in both eyes (figure). Results of OCT-angiography and ganglionar cells complex analysis

appeared normal. Furthermore, four patients presented subtle cotton wool spots and microhaemorrhages along the retinal arcade, observed on fundus examination, color fundus photography, and red-free imaging. Visual acuity and pupillary reflexes were normal in all eyes, and we detected no symptoms or signs of intraocular inflammation.

Although animal models suggest ocular lesions could include retinitis and optic neuritis, this is, to the best of our knowledge, the first report of retinal findings possibly associated with COVID-19 infection in humans. Ganglion cell and plexiform layer findings could be associated with CNS manifestations that have been described in animal studies⁴ and in COVID-19 neurological events.

5. 由 SARS-CoV-2 感染引起的噬血细胞性淋巴组织细胞增生症：结合临床和实验室特征相关性的系列尸检

SARS-CoV-2 Infection Associated Hemophagocytic Lymphohistiocytosis: An autopsy series with clinical and laboratory correlation

来源: medRxiv

发布时间: 2020-05-12

链接: <https://www.medrxiv.org/content/10.1101/2020.05.07.20094888v1>

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DOI 或 PUBMED ID:

编译者: 宋珂

中文摘要:

背景: 有一部分 COVID-19 患者存在细胞因子风暴的临床特征。但是, 尚未有诊断出噬血细胞性淋巴组织细胞增生症 (HLH) 的临床病理特征报道。迄今为止, 病理学研究主要集中在发现肺部的弥漫性肺泡损害 (DAD)。因此, 作者对 4 名因患 COVID-19 而连续死亡的患者网状内皮组织器官进行了研究, 并结合临床和实验室参数一起检测 HLH。

方法: 对 4 名因患 COVID-19 而死亡的患者进行了仅限于胸部和腹部的尸检。所有病例均对脾脏, 肝脏和多个肺门/纵隔淋巴结进行了采样。并使用肋骨挤压的方式采集了部分病例的骨髓样本。对样本进行了常规的 H&E 染色以及针对 CD163 的免疫组化染色, 用来检测噬血细胞现象。使用死亡前血液样本的临床和实验室记录计算 H 评分。

发现: 4 例患者的肺部均出现 DAD。其中 3 例在肺门/纵隔淋巴结内存在噬血细胞现象的组织学证据。1 例在脾脏中存在噬血细胞现象, 而在肝脏或骨髓中则没有发现。已发现的噬血细胞现象主要表现为淋巴细胞吞噬现象。一名患者表现出 HLH 的诊断特征, 其 H 评分为 217。而另一名患者由于缺少甘油三酸酯水平记录, 其部分 H 评分为 145, 因而可能存在 HLH。两名患者均出现高烧和早期血清铁蛋白升高。然而, 两者均未观察到两系血细胞减少, 全血细胞减少和低纤维蛋白原血症。其余两名患者的 H 评分为 131 和 96。

说明: 这是对由 SARS-CoV-2 引起的 HLH 的首个研究报告。在一部分患有严重 COVID-19 的患者中鉴定出 HLH, 为制定治疗策略的临床试验提供了信息。

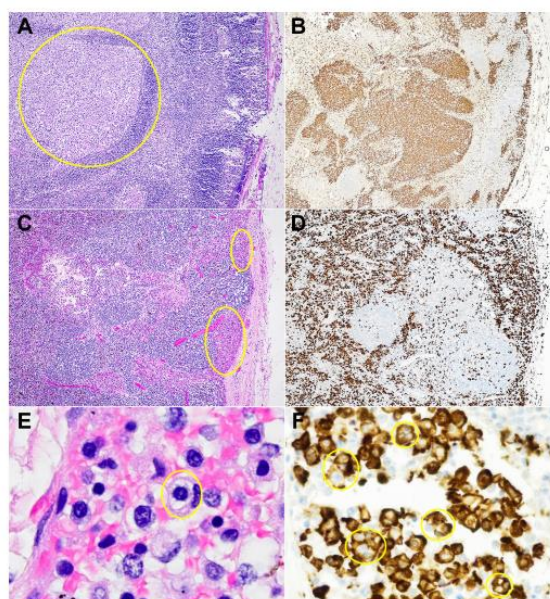


Figure 1. Hemophagocytosis in pulmonary hilar and mediastinal lymph nodes. (A/B) H&E and CD163 immunohistochemical stains of lymph node from patient 1 showing distended cortical and subcortical sinusoids filled with histiocytes exhibiting focal necrosis. (C/D) H&E and CD163 immunohistochemical stains of a lymph node from patient 2 showing a lesser degree of sinusoidal expansion, predominantly filling the subcapsular sinuses. Hemophagocytosis consisted predominantly of lymphophagocytosis in all cases and seen on (E) H&E stain and highlighted with (F) CD163 immunohistochemical stain where numerous histiocytes phagocytosing one to several lymphocytes were apparent

Abstract:

Background: A subset of COVID-19 patients exhibit clinical features of cytokine storm. However, clinicopathologic features diagnostic of hemophagocytic lymphohistiocytosis (HLH) have not been reported. Pathologic studies to date have largely focused on the pulmonary finding of diffuse alveolar damage (DAD). To this aim, we study the reticuloendothelial organs of four consecutive patients dying of COVID-19 and correlate with clinical and laboratory parameters to detect HLH.

Methods: Autopsies restricted to chest and abdomen were performed on four patients who succumbed to COVID-19. Spleen, liver, and multiple pulmonary hilar/mediastinal lymph nodes were sampled in all cases. Bone marrow was obtained by rib squeeze in a subset of cases. Routine H&E staining as well as immunohistochemical staining for CD163 was performed to detect hemophagocytosis. Clinical and laboratory results from pre-mortem blood samples were used to calculate H-scores.

Findings: All four cases demonstrated DAD within the lungs. Three of the four cases had histologic evidence of hemophagocytosis within pulmonary hilar/mediastinal lymph nodes. One case showed hemophagocytosis in the spleen but none showed hemophagocytosis in liver or bone marrow. Lymphophagocytosis was the predominant form of hemophagocytosis observed. One patient showed diagnostic

features of HLH with an H-score of 217 while a second patient was likely HLH with a partial H-score of 145 due to missing triglyceride level. Both patients exhibited high fever and early onset rise in serum ferritin; however, neither bicytopenia, pancytopenia, nor hypofibrinogenemia were observed in either. The remaining two patients had H-scores of 131 and 96.

Interpretation: This is the first report of SARS-CoV-2 associated HLH. Identification of HLH in a subset of patients with severe COVID-19 will inform clinical trials of therapeutic strategies.

6. 心力衰竭患者血浆 ACE2 浓度及肾素-血管紧张素-醛固酮系统抑制剂的影响

Circulating Plasma Concentrations of Angiotensin-Converting Enzyme 2 in Men and Women with Heart Failure and Effects of Renin-Angiotensin-Aldosterone Inhibitors

来源: Eur Heart J

发布时间: 2020-05-10

链接: <https://pubmed.ncbi.nlm.nih.gov/32388565/>

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DOI 或 PUBMED ID: 10.1093/eurheartj/ehaa373.

编译者: 张丽双

中文摘要:

目的: 目前流行性冠状病毒 SARS-CoV-2 感染的人群年龄较大, 但主要是老年人, 特别是男性和心血管疾病患者。最近的报道表明肾素-血管紧张素-醛固酮系统 (RAAS) 抑制剂的使用与之相关。血管紧张素转换酶 2 (ACE2) 是冠状病毒的功能性受体。较高的 ACE2 浓度可能会增加使用 RAAS 抑制剂患者对 SARS-CoV-2 的敏感性。

方法: 对 1485 名男性和 537 名女性心力衰竭患者进行 ACE2 浓度测定 (索引队列 index cohort)。结果在 1123 名男性和 575 名女性中得到验证 (验证队列)。

结果: 男性的中位年龄为 69 岁, 女性为 75 岁。两组队列中 ACE2 浓度升高的最强预测因子均为男性 (估计值分别为 0.26, $P < 0.001$ 和 0.19, $P < 0.001$)。在指数队列中, 使用 ACE 抑制剂、血管紧张素受体阻滞剂 (ARB) 或盐皮质激素受体拮抗剂 (MRA) 不是血浆 ACE2 的独立预测因子。在验证队列中, ACE 抑制剂 (估计值 = -0.17, $P = 0.002$) 和 ARB 使用 (估计值 = -0.15, $P = 0.03$) 是低血浆 ACE2 的独立预测因子, 而 MRA (估计值 = 0.11, $P = 0.04$) 是高血浆 ACE2 浓度的独立预测因子。

结论: 在两组独立的心力衰竭患者中, 男性血浆 ACE2 浓度高于女性, 但使用 ACE 抑制剂和 ARB 均与较高的血浆 ACE2 浓度无关。这些数据可能解释了 COVID-19 在男性中较高的发病率和死亡率, 但不支持先前的报告, 即 ACE 抑制剂或 ARB 通过增加血浆 ACE2 浓度增加 COVID-19 的脆弱性。

Abstract:

Aims: The current pandemic coronavirus SARS-CoV-2 infects a wide age group but predominantly elderly individuals, especially men and those with cardiovascular disease. Recent reports suggest an association with use of renin-angiotensin-

aldosterone system (RAAS) inhibitors. Angiotensin-converting enzyme 2 (ACE2) is a functional receptor for coronaviruses. Higher ACE2 concentrations might lead to increased vulnerability to SARS-CoV-2 in patients on RAAS inhibitors.

Methods: We measured ACE2 concentrations in 1485 men and 537 women with heart failure (index cohort). Results were validated in 1123 men and 575 women (validation cohort).

Results: The median age was 69 years for men and 75 years for women. The strongest predictor of elevated concentrations of ACE2 in both cohorts was male sex (estimate = 0.26, $P < 0.001$; and 0.19, $P < 0.001$, respectively). In the index cohort, use of ACE inhibitors, angiotensin receptor blockers (ARBs), or mineralocorticoid receptor antagonists (MRAs) was not an independent predictor of plasma ACE2. In the validation cohort, ACE inhibitor (estimate = -0.17, $P = 0.002$) and ARB use (estimate = -0.15, $P = 0.03$) were independent predictors of lower plasma ACE2, while use of an MRA (estimate = 0.11, $P = 0.04$) was an independent predictor of higher plasma ACE2 concentrations.

Conclusion: In two independent cohorts of patients with heart failure, plasma concentrations of ACE2 were higher in men than in women, but use of neither an ACE inhibitor nor an ARB was associated with higher plasma ACE2 concentrations. These data might explain the higher incidence and fatality rate of COVID-19 in men, but do not support previous reports suggesting that ACE inhibitors or ARBs increase the vulnerability for COVID-19 through increased plasma ACE2 concentrations.

编者注:

该文中采用了来自于 BIOSTAT-CHF 项目的人群队列。ACE2 采用质谱技术测量。

7. 雄激素既调节 SARS-CoV-2 受体水平，又与男性的严重 COVID-19 症状相关

Androgen Regulates SARS-CoV-2 Receptor Levels and Is Associated with Severe COVID-19 Symptoms in Men

来源: bioRxiv

发布时间: 2020-05-12

链接: <https://www.biorxiv.org/content/10.1101/2020.05.12.091082v1>

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中文摘要:

SARS-CoV-2 感染已导致全球性健康危机，但对疾病的病理生理学和潜在治疗方案的了解仍然有限。SARS-CoV-2 感染是通过病毒刺突蛋白与宿主细胞膜上的血管紧张素转化酶 2 (ACE2) 结合和内化而发生。致命的并发症是由表达高水平 ACE2 的重要器官 (包括肺，心脏和肾脏) 的损伤和衰竭引起的。文中作者建立了一种高通量药物筛选策略，以鉴定可降低人胚胎干细胞 (hESC) 衍生的心肌细胞中 ACE2 水平的治疗候选药物。包括 5 种 α 还原酶抑制剂在内的经过验证的命中化合物的药物靶标分析表明，雄激素信号是 ACE2 水平的关键调节剂。用 5 α 还原酶抑制剂度他雄胺治疗，可降低 hESC 来源的心肌细胞与人肺泡上皮细胞

ACE2 水平和重组刺突受体结合域的内化。最后，关于 COVID-19 患者的临床数据表明，根据血清肌钙蛋白 T 水平的测定，异常的雄激素状态与严重的疾病并发症和心脏损伤显著相关。这些发现为男性 COVID-19 患者疾病易感性增加的机制提供了重要的见识，并确定雄激素受体抑制是一种潜在的治疗策略。

Abstract:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has led to a global health crisis, and yet our understanding of the disease pathophysiology and potential treatment options remains limited. SARS-CoV-2 infection occurs through binding and internalization of the viral spike protein to angiotensin converting enzyme 2 (ACE2) on the host cell membrane. Lethal complications are caused by damage and failure of vital organs that express high levels of ACE2, including the lungs, the heart and the kidneys. Here, we established a high-throughput drug screening strategy to identify therapeutic candidates that reduce ACE2 levels in human embryonic stem cell (hESC) derived cardiac cells. Drug target analysis of validated hit compounds, including 5 alpha reductase inhibitors, revealed androgen signaling as a key modulator of ACE2 levels. Treatment with the 5 alpha reductase inhibitor dutasteride reduced ACE2 levels and internalization of recombinant spike receptor binding domain (Spike-RBD) in hESC-derived cardiac cells and human alveolar epithelial cells. Finally, clinical data on coronavirus disease 2019 (COVID-19) patients demonstrated that abnormal androgen states are significantly associated with severe disease complications and cardiac injury as measured by blood troponin T levels. These findings provide important insights on the mechanism of increased disease susceptibility in male COVID-19 patients and identify androgen receptor inhibition as a potential therapeutic strategy.

8. 在重症 COVID19 成年住院患者中使用托珠单抗的早期结果：一项来自瓦尔德希布伦大学医院的前瞻性队列研究的初步报告

Early outcomes of tocilizumab in adults hospitalized with severe COVID19. An initial report from the Vall d'Hebron COVID19 prospective cohort study.

来源: medRxiv

发布时间: 2020-05-14

链接: <https://www.medrxiv.org/content/10.1101/2020.05.07.20094599v1>

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编译者: 孔娟

中文摘要:

背景: 在 COVID19 大流行的背景下，调节免疫系统以防止肺损伤正被广泛用于对抗 COVID19 的治疗。

方法: 作者报告了在西班牙巴塞罗那瓦尔德希布伦大学医院进行的一项前瞻性队列研究的初步结果, 包括所有连续确诊感染 SARS-CoV2 并在 3 月 25 日前接受托珠单抗治疗的患者。研究的主要终点是给予托珠单抗治疗后 7 天的死亡率。次要终点是重症监护病房的入院、急性呼吸窘迫综合征的发展和呼吸功能不全等。

结果: 82 名 COVID19 患者接受了至少一剂托珠单抗。平均(标准差)年龄为 59.1 (19.8) 岁, 63%为男性, 22%为非西班牙血统, 中位数(IQR)根据年龄调整后的查尔森指数为 3 (1 至 4) 点。分别有 62 名(75.6%)和 45 名(54.9%)患者出现呼吸衰竭和急性呼吸窘迫综合征。从症状发作到急性呼吸窘迫综合征发展的中位时间为 8 (5-11) 天。从症状发作到首次给药的平均时间为 9 (7-11) 天。在接受托珠单抗治疗炎症相关肺损伤的 COVID-19 患者中, 7 天死亡率为 26.8%。死亡率的危险比为 3.3; 95%可信区间为 1.3 至 8.5 (年龄调整后死亡率的风险比为 2.1; 95%可信区间为 0.8 至 5.8)。

结论: 从肺损伤开始到给予托珠单抗的时间对患者的康复至关重要。在临床试验获得更多数据之前, 作者的结果可能有助于一线医生在资源稀缺时做出循证决策, 并实施公平透明的分配程序, 最大限度地提高干预的效率。

Abstract:

Background: Modulation of the immune system to prevent lung injury is being widely used against the new coronavirus disease (COVID19) despite the scarcity of evidence.

Methods: We report preliminary results from the Vall dHebron prospective cohort study at Vall dHebron University Hospital, in Barcelona (Spain), including all consecutive patients who had a confirmed infection with the severe acute respiratory syndrome coronavirus2 (SARSCoV2) and who were treated with tocilizumab until March 25th. The primary endpoint was mortality at 7 days after tocilizumab administration. Secondary endpoints were admission to the intensive care unit, development of ARDS and respiratory insufficiency among others.

Results: 82 patients with COVID19 received at least one dose of tocilizumab. The mean (SD) age was 59.1 (19.8) years, 63% were male, 22% were of non Spanish ancestry, and the median (IQR) age adjusted Charlson index at baseline was 3 (1 to 4) points. Respiratory failure and ARDS developed in 62 (75.6%) and 45 (54.9%) patients, respectively. Median time from symptom onset to ARDS development was 8 (5 to 11) days. The median time from symptom onset to the first dose of tocilizumab was 9 (7 to 11) days. Mortality at 7 days was 26.8%. Hazard ratio for mortality was 3.3; 95% CI, 1.3 to 8.5 (age adjusted hazard ratio for mortality 2.1; 95% CI, 0.8 to 5.8) if tocilizumab was administered after the onset of ARDS.

Conclusion: Time from lung injury onset to tocilizumab administration may be critical to patient recovery. Our preliminary data could inform bedside decisions until more data from clinical trials becomes available.

编者注:

该临床试验没有对照, 有效性只能和其他没有严格对照的数据进行比较。

4 月 28 日的一项来自法国的新闻宣传一个未完成的有对照临床试验中, 托珠单抗显示出明显效果 <https://medicalxpress.com/news/2020-04-arthritis-drug-significant->

[severe-covid-.html](#)。包括罗氏、genetech, 赛诺菲等公司都在开展自己公司 IL-6 抑制剂的 COVID-19 临床试验。我们拭目以待。不过该药价格不菲, 每针高达 800 美元。

9. FDA 于 5 月 12 日批准 Moderna 的 mRNA 疫苗(mRNA-1273)进入审批快速通道

Moderna Receives FDA Fast Track Designation for mRNA Vaccine (mRNA-1273) Against Novel Coronavirus

来源: <https://investors.modernatx.com/news-releases/news-release-details/moderna-receives-fda-fast-track-designation-mrna-vaccine-mrna>

10. COVID-19 病人支气管免疫细胞的单细胞图谱

Single-cell landscape of bronchoalveolar immune cells in patients with COVID-19

来源: Nature Medicine

发布时间: 2020-05-1

文章链接: <https://www.nature.com/articles/s41591-020-0901-9>

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DOI 或 PUBMED ID:10.1038/s41591-020-0901-9

编译者: 蒋立春

中文摘要:

研究者们对不同严重程度 COVID-19 病人的支气管肺泡灌洗液免疫细胞进行了单细胞测序, 并且和已经发表的健康人的对应单细胞测序进行了比较分析。该研究发现重症 COVID-19 病人的支气管肺泡灌洗液中富含炎性的由单核细胞来源的巨噬细胞。中度症状的病人的特征是存在高度克隆扩增的 CD8⁺ 的 T 细胞。支气管免疫微环境提示了 COVID-19 重症病人的发病和恢复的内在机理。

Abstract:

Respiratory immune characteristics associated with Coronavirus Disease 2019 (COVID-19) severity are currently unclear. We characterized bronchoalveolar lavage fluid immune cells from patients with varying severity of COVID-19 and from healthy people by using single-cell RNA sequencing. Proinflammatory monocyte-derived macrophages were abundant in the bronchoalveolar lavage fluid from patients with severe COVID-19. Moderate cases were characterized by the presence of highly clonally expanded CD8⁺ T cells. This atlas of the bronchoalveolar immune microenvironment suggests potential mechanisms underlying pathogenesis and recovery in COVID-19.

11. 血清蛋白质谱揭示了早期 COVID-19 感染的炎症和免疫信号

Serum protein profiling reveals a landscape of inflammation and immune signaling in early-stage COVID-19 infection

来源: medrxiv

发布时间: 2020.05.13

文章链接: <https://www.medrxiv.org/content/10.1101/2020.05.08.20095836v1>

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中文摘要:

2019 冠状病毒病 (COVID-19) 是一种高度传染性疾病, 威胁着世界各国人民的生命安全。在 COVID-19 患者病情严重转变过程中, 血液中细胞因子的升高是诱发细胞因子风暴和免疫抑制的关键。然而, 在整个 SARS-CoV-2 感染过程中, COVID-19 患者血清蛋白的综合变化尚不清楚。在这项工作中, 他们开发了高密度抗体芯片, 并对早期 COVID-19 (n=15) 和流感 (n=13) 患者的血清样本进行了深入的蛋白质组学分析。他们鉴定了一组大的差异表达蛋白 (n=125), 这些蛋白参与了与 SARS-CoV-2 感染相关的炎症和免疫信号通路。此外, 中性粒细胞和淋巴细胞与 CCL2 和 CXCL10 介导的细胞因子信号通路显著相关。这些信息对于理解 COVID-19 的发病机制、识别生物标志物和开发最佳抗炎治疗具有重要价值。

Abstract:

Coronavirus disease 2019 (COVID-19) is a highly contagious infection and threatening the human lives in the world. The elevation of cytokines in blood is crucial to induce cytokine storm and immunosuppression in the transition of severity in COVID-19 patients. However, the comprehensive changes of serum proteins in COVID-19 patients throughout the SARS-CoV-2 infection is unknown. In this work, we developed a high-density antibody microarray and performed an in-depth proteomics analysis of serum samples collected from early COVID-19 (n=15) and influenza (n=13) patients. We identified a large set of differentially expressed proteins (n=125) that participate in a landscape of inflammation and immune signaling related to the SARS-CoV-2 infection. Furthermore, the significant correlations of neutrophil and lymphocyte with the CCL2 and CXCL10 mediated cytokine signaling pathways was identified. These information are valuable for the understanding of COVID-19 pathogenesis, identification of biomarkers and development of the optimal anti-inflammation therapy.

12. 感染 SARS-CoV-2 的猕猴发生呼吸系统疾病

Respiratory disease in rhesus macaques inoculated with SARS-CoV-2

<https://www.nature.com/articles/s41586-020-2324-7>

3月23日简报第9条报道过该研究的预印本。

13. 一个适用于小鼠的 SARS-CoV-2 模型，用于评估针对 COVID-19 的理疗措施

A mouse-adapted SARS-CoV-2 model for the evaluation of COVID-19 medical countermeasures

<https://www.biorxiv.org/content/10.1101/2020.05.06.081497v1.full.pdf>

这篇文章报道了对 S 蛋白 498 和 499 位的改造，让 SARS-CoV-2 适应小鼠，构建了小鼠的感染和发病模型。参考 5 月 6 日简报 12 条，姜世勃和合作课题组通过自然 6 代筛选，筛选到一株 S 蛋白 501 位突变的感染小鼠的 SARS-CoV-2 病毒株。