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COVID-19与心血管疾病

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摘　要

冠状病毒(CoVs)是单链正股RNA病毒，具有快速突变和重组的能力。冠状病毒已知会导致人类和动物的呼吸道或肠道感染。急性呼吸道感染，包括流感、呼吸道病毒和细菌性肺炎，是公认的心血管疾病(CVD)的诱因，而潜在的CVD通常与合并症有关，这可能会增加传染病的发病率和严重程度。导致2019年冠状病毒(COVID-19)已迅速发展成大流行，据报告，大部分受影响的患者患有潜在的心血管疾病。在本综述中，我们简要回顾了冠状病毒的基本知识、对心脏损害的发病机制、临床表现及其相关的心血管并发症。我们对COVID-19的了解仍在迅速发展，以进一步深入了解冠状病毒对心血管系统的影响。了解COVID-19对心血管系统的影响对于为心脏病患者提供全面的医疗服务非常关键。

关键词

COVID-19，发病机制，临床表现，心血管并发症，心血管疾病

COVID-19 and Cardiovascular Disease

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Abstract

Coronavirus (CoVs) is a single-stranded positive stranded RNA virus with the ability of rapid mutation and recombination. Coronaviruses are known to cause respiratory or intestinal infections in humans and animals. Acute respiratory infections, including influenza, respiratory viruses and bacterial pneumonia, are recognized as cardiovascular diseases (CVD). While underlying CVD are

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often associated with cardiovascular complication which may increase the incidence and severity of infectious diseases. The virus that caused the coronavirus (COVID-19) in 2019 has rapidly evolved into a pandemic, with most of the affected patients reported to have suffered from potential cardiovascular diseases. In this review, we briefly review the basic knowledge of coronaviruses, their pathogenesis of cardiac damage, clinical manifestations and related cardiovascular complications. Our understanding of COVID-19 is still evolving rapidly to further our understanding of the effects of coronavirus on the cardiovascular system. Understanding the effects of COVID-19 on the cardiovascular system is critical to providing comprehensive health care to patients with heart disease.

Keywords

COVID-19, Pathogenesis, Clinical Manifestations, Cardiovascular Complication, Cardiovascular Disease

1. 冠状病毒的概念

冠状病毒是微型的大小(直径 60~140 纳米)，含有单个正链核糖核酸(RNA)，通常长度从 26 到 32 kbs 不等。SARS-CoV-2 是一种新型的 β 冠状病毒类别，具有圆形或椭圆形的多态性形式。下一代测序的计量学分析表明，该病毒由冠状病毒常见的六种主要开放读取码(ORF)和许多其他辅助基因组成[1]。进一步分析表明，一些表达的基因与早期 SARS-CoV 的核苷酸序列特征共享不到 80% [2]。SARS-CoV-2RNA 基因组含有 29,891 个核苷酸，编码为 9860 个氨基酸[2]。虽然它可能的起源还没有完全了解，但基因组分析表明，它可能是从蝙蝠中发现的菌株进化而来的[3] [4]。与大多数其他冠状病毒类似，SARS-Cov-2 的外膜糖蛋白与宿主细胞靶点受体(如 ACE2、CD26、Ezrin、环素)相互作用，对细胞粘附和毒性很重要[5]。在电子显微镜下，SARS-CoV-2 表面形态具有多种多蛋白、核蛋白和膜蛋白，如尖峰糖蛋白 S [6]。后者涉及远离病毒表面的同质体，给它一个光环，外观或如日冕。

2. COVID-19 与心血管系统有关的发病机制

SARS-CoV-2 似乎会损害心脏的肌肉组织，并可能导致心肌炎[7]。因此，在 SARS-CoV-2 感染后，报告了各种收缩功能降低的严重心肌炎病例[8]。虽然 COVID-19 的心肌介入机制仍在研究之中，但它们可能包括直接病毒感染、缺氧引起的凋亡和体内与细胞因子风暴相关的细胞损伤[9]。过度炎症(IL6、TNF®和 IL-1)可以进一步调节多个心肌细胞离子通道的功能，特别是 K+和 Ca+通道，导致炎症性心脏通道病变[10]。细胞内钙过量促进心肌细胞凋亡[11]。此外，心肌损伤可能是这些患者心律失常风险增加的主要驱动因素[12]。随着 COVID-19 与 CV 系统之间相互作用的不断演变，现有临床数据显示，8%至 28%的 COVID-19 感染患者将表现出急性心脏损伤。此情况通过增加心脏生物标志物释放，如高蛋白 I (TnT)，N 终端亲脑营养肽(NT-proBNP)或 B 型尿素肽(BNP) [13] [14] [15]。建议提供心肌损伤的证据，理由是 COVID-19 患者的 TnT 升高与致命结果显著相关[16]。许多机制可以阐明这种现象主要是病毒性心肌炎，细胞因子驱动的心肌损伤，和微心肌病。然而，这些机制都没有被确认为肌肽上升和/或心肌损伤的关键驱动因素。此外，鉴于 ACE2 在心肌细胞中的大量分布[17]，有人建议，心肌炎可能阐明 TnT 在某些情

况下的上升，主要是急性左心室衰竭在某些情况下[16] [18]。值得注意的是，心脏 TnT 的上升不应被视为急性 MI 的证据[19]。这应该基于临床评估和心电图，其中心脏 TnT 的心脏肌肽高程可以通知与 COVID-19 相关的一些心脏疾病的诊断[18]。提升的 TnT 可能是多因素的，不太可能归因于动脉冠状动脉闭塞[19]。事实上，16%的底层 CVD 患者，但与正常的 TnT 水平有一个相对有利的结果[14]。关于心脏生物标志物作用的现有数据支持评估 TnT 和营养肽(NT-proBNP 和 BNP)对严重 COVID-19 患者心脏风险分层和预后的作用[20]，基于心肌损伤的证据和 CV 并发症的存在，这可能改善 COVID-19 患者的 CV 护理，以及降低感染风险，但可能会有一些限制[21]。然而，在 COVID-19 的 CV 疾病诊断、风险分层和管理方面，还需要额外的新型生物标志物。

3. 与 COVID-19 感染相关的心血管并发症

3.1. 心肌损伤和心肌炎

先前的病毒性疾病，包括中东呼吸综合征冠状病毒(MERS-CoV)，与心肌损伤和心肌炎有关，其高程被认为是由于心脏生理压力增加、缺氧或直接心肌损伤[7] [12] [22]。首批报告与 SARS-CoV-2 相关的心肌损伤是对中国武汉 41 名被诊断为 COVID-19 的患者的研究，其中 5 例患者(12%)有一个高灵敏度的肌肽 I 高于 28 pg/mL 的阈值[9]。随后的研究发现，在 7%~17%的 COVID-19 住院患者和 22%~31%的重症监护病房(ICU)住院的患者中，肌肽水平升高的心肌损伤可能发生[13] [15] [23]。心肌炎也已被确定与高病毒载量和单核渗透识别在解剖一些患者的 COVID-19 [7] [24] [25]，事实上，一项研究表明，高达 7%的 COVID-19 相关死亡是由于心肌炎[26]。

急性心肌炎呈现在可变的临床严重程度范围内，是 COVID-19 时代的一个重要诊断挑战。COVID-19 患者可能出现胸痛、呼吸困难、心律失常和急性左心室功能障碍[13] [15] [23] [26] [27]。在心肌炎和心肌损伤患者中，血清肌肽值将异常。心电图(ECG)可以证明一系列发现，在某些情况下模仿急性冠状动脉综合征(ACS)。心电图异常由心肌炎症引起，包括非特定的 ST 段-T 波异常、T 波反转、PR 段和 ST 段偏差(凹陷和高程)。鼓励心电图和心脏病学咨询，如果其中任何一个可用，因为区分心肌炎和 ACS 是困难的。回声心动图评估更有可能显示焦点壁运动异常与活跃，显著的 ACS，而严重的 COVID-19 相关心肌炎将显示要么没有壁运动缺陷或全球壁运动功能障碍[28]。心电图和回声心动图异常在 COVID-19 的设置是疾病严重程度的标记，并与更坏的结果相关[16] [29]。此外，COVID-19 感染患者的肌肽升高与严重感染(包括死亡率)患者出现不良后果的风险增加有直接关系[14] [30] [31]。

3.2. 急性心肌梗死

严重的全身炎症会增加动脉粥样硬化斑块中断和 AMI 的风险[14] [22] [28] [32] [33]。2018 年的一项研究发现，流感和其他选定的病毒性疾病与疾病诊断后头 7 天内 AMI 风险增加有关，流感发病率为 6.1，其他病毒的发病率为 2.8 [33]。另一项针对因社区获得性肺炎住院的患者的研究发现，住院后持续数年的活性心疾病风险增加[30]。由于广泛的炎症和高凝血性，AMI 的风险可能存在于 COVID-19 患者中[12] [28]。

3.3. 急性心力衰竭

急性心力衰竭可能是 COVID-19 感染的主要表现。一项研究发现，23%的患者在首次呈现 COVID-19 时可能出现急性心力衰竭，33%的患者出现心肌病[15]。另一项研究发现，24%的患者存在心力衰竭，与死亡率增加有关[22]。目前还不知道心力衰竭是否由于新的心肌病与先前未确诊的心力衰竭的恶化[34]。在管理静脉输液时，必须意识到这种潜在的心脏功能障碍，避免过度侵入性液体置换。重要的是，右心

力衰竭也可能发生，特别是在那些有 ARDS 和急性肺损伤的人中[12] [35]。

3.4. 心律失常

心绞痛可能是超过 7%的 COVID-19 患者的症状[24]。在 COVID-19 感染的患者中，已经遇到一系列的呼吸困难。最常见的情况是，鼻窦心动过速在此类患者中出现，由多种同时原因(输液、发烧、缺氧、焦虑等)导致[12]。一项研究发现，17%的住院患者和 44%的 ICU 患者患有 COVID-19 [23]。由于缺氧、炎症性应激和新陈代谢异常，在病毒性疾病的环境中可能发生心律失常。如果血清肌张力障碍与血清肌肽升高有关，临床医生应在差分诊断中考虑心肌损伤、急性心肌炎和 ACS [12]。

3.5. 静脉血栓事件

COVID-19 患者患 VTEs 的风险也增加[36] [37]。全身炎症、异常凝固状态、多机能功能障碍和危重疾病都是导致 VTE 风险增加的潜在因素[15] [35] [37] [38] [39]。研究表明，COVID-19 患者的凝血途径异常，包括 D-dimer 显著升高等[13] [15] [35] [37] [38] [39]。一项对 25 名 COVID-19 肺炎患者的研究发现，所有中位数为 6.06 微克/毫升的患者都存在 D-dimer 升高，其中 10 名患者在计算机断层扫描肺血管造影(CTPA)上诊断出肺栓塞(PE) [38]。CTPA 上确诊 PE 的患者表现出 D-dimer 中位数水平为 11.07 微克/毫升[23]。在 COVID-19 感染患者住院期间(赔率比 18.4)中，D-dimer 水平大于 1 微克/mL 与死亡风险增加有关[15]。一项研究表明，抗凝，主要是低分子量肝素，可能与降低死亡率在严重的 COVID-19 感染或那些 D-dimer 大于正常上限六倍有关[40]。

4. 结论

COVID-19 主要是肺部疾病，高过敏性免疫反应，或“细胞因子风暴”，具有全身性影响。此外 COVID-19 的预后可能因预先存在的心血管疾病而恶化，或者即使没有相关历史，COVID-19 也能诱发急性心血管事件。它们包括以局部(即肺)或全身弥散性血管内凝血功能障碍形式表现出形成血栓的可能性。我们对 COVID-19 的了解仍在迅速发展，以进一步深入了解冠状病毒对心血管系统的影响。目前新出现的德尔塔病毒对心脏的损害，是否与新冠病毒相似，值得我们关注。

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