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Поражение сердца при COVID-19: вопросы патогенеза и диагностики

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АННОТАЦИЯ

Тема коронавирусной инфекции до настоящего времени не теряет своей актуальности в медицинской среде. Среди гетерогенных клинических проявлений этого заболевания выделяют поражение структур сердца, главным образом воспалительного характера. Помимо миокардита, при коронавирусной инфекции возможен целый спектр острых или отсроченных поражений сердца, в частности острый коронарный синдром, тромбоэмболические события, сердечная недостаточность, нарушения ритма сердца. Известно, что прогноз для пациентов с поражением сердца значимо ухудшается. Своевременная постановка диагноза и начало лечения играют принципиально важную роль для предотвращения тяжёлых осложнений.

В обзоре приводятся современные литературные данные о патогенезе поражения сердца при COVID-19, обсуждаются вопросы рациональной диагностики данной патологии с помощью современных методик (лабораторных, функциональных, визуализирующих), в том числе инвазивных. Главную роль среди визуализирующих методов играет магнитно-резонансная томография сердца с контрастированием. В настоящее время признано, что диагностика миокардита, ассоциированного с коронавирусной инфекцией, имеет ряд принципиальных отличий от диагностики миокардита другой природы. Кроме того, отражены основные аспекты воспалительного поражения сердца, ассоциированного с вакцинацией против COVID-19, поскольку такое осложнение возникает чаще, чем принято считать. Нередко оно является поводом для отказа от вакцинации, что может повлечь за собой тяжёлые последствия как для отдельного человека, так и популяции в целом.

Ключевые слова: COVID-19; миокардит; острый коронарный синдром; нарушения ритма сердца; магнитно-резонансная томография; вакцинация.

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COVID-19-related cardiac lesion: The questions of pathogenesis and diagnostics

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ABSTRACT

Coronavirus infection is still a topic of interest in the medical community today. Among the heterogeneous clinical manifestations of this disease, lesions of cardiac structures often occur. They are mainly inflammatory in nature and can be acute or delayed. Aside from myocarditis, coronavirus infection can induce cardiac injuries, including acute coronary syndrome, thromboembolic events, heart failure, and heart rhythm disturbances. It is well known that the prognosis for patients with cardiac lesions significantly worsens; timely diagnosis and treatment initiation play an important role in preventing severe complications. This review presents the most recent literature data on the pathogenesis of cardiac lesions in COVID-19 patients and discusses the rational diagnosis of this pathology using modern techniques, such as laboratory, functional imaging (cardiac magnetic resonance is the most important of these), and invasive ones. It is now established that diagnosing myocarditis caused by coronavirus infection differs fundamentally from diagnosing other types of myocarditis. Furthermore, the main aspects of inflammatory heart lesions associated with COVID-19 vaccination are discussed, as this complication occurs more frequently than is commonly believed. It is often used as a rationale for refusing vaccination; however, this decision may severely affect the individual and the population.

Keywords: acute coronary syndrome; COVID-19; heart rhythm disturbances; magnetic resonance imaging; myocarditis; vaccination.

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COVID-19的心脏受损： 发病机制和诊断的问题（科学综述）

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简评

冠状病毒感染仍然是医学界的一个热门话题。心脏结构受损从该病的异质性临床表现中脱颖而出，主要是炎性的。除心肌炎外，冠状病毒感染还可导致一系列急性或迟发性的心脏受损，如急性冠状动脉综合征、血栓栓塞性事件、心力衰竭和心律失常。众所周知，有心脏受损的病人的预后大幅度恶化。及时诊断和启动治疗对于严重并发症的预防至关重要。

本综述介绍了与COVID-19心脏受损发病机制有关的现代文献资料，讨论了利用现代技术（实验室、功能、影像学），包括侵入性技术，对这种病理进行合理诊断的问题。在影像技术中起主要作用的是心脏超影磁共振成像。现在专家认为，与冠状病毒感染有关的心肌炎诊断，与其他心肌炎诊断相比，有一些根本区别。此外，还反映了与COVID-19疫苗接种相关的炎症性心脏受损的主要方面，因为这种并发症的发生率比通常认为的高。它往往是不打疫苗的一个理由，这对个人和整个人群都会产生严重的后果。

关键词：COVID-19；心肌炎；急性冠状动脉综合征；心律失常；磁共振成像；疫苗接种。

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绪论

由SARS-CoV-2病毒引起的冠状病毒感染于2019年12月首次被发现。这种病毒感染在短时间内在全球迅速蔓延。该疾病的临床表现范围涵盖流感综合征的所有症状，包括咳嗽、寒热、乏力、呼吸困难、嗅觉丧失、味觉缺失和咽痛。这些症状可能发展为急性呼吸窘迫综合征和多器官衰竭。此外，心脏结构（主要是心肌）的急性受损也可能是该病的后果之一。许多研究表明了，高肌钙蛋白水平与冠状病毒感染患者的死亡率增加有关。及时准确地诊断这种疾病对患者的生存至关重要。但迄今为止，这种诊断仍是一项挑战。

本综述旨在批判性地总结COVID-19相关心肌炎的现代数据，以及研究其发病机制和鉴别诊断的主要方面。

集合了来自科学文章数据库PubMed的文章来撰写手稿。检索词为“COVID-19/SARS-CoV-2 and myocardit*”的句子组合。这些组合必须出现在文章的标题中。为此，[ti]被添加到检索标准中。作者只选择了全文文章：荟萃分析、系统综述和评论。这些条件是用适当的筛选器指定的。在上述表述中添加“and vaccin*”，以选择关于接种疫苗后引发的心肌炎的文献。其余检索参数与上述参数类似。

经过筛选后，126篇文章被纳入文献综述的初始样本，其中67篇文章讨论了冠状病毒疫苗接种的问题。

COVID-19的心脏受损

冠状病毒感染（COVID-19）是一种由SARS-CoV-2病毒引起的疾病。该病毒于2019年底在中国武汉市首次发现，并迅速蔓延到了世界各地，引起大流行。

该病的症状多种多样，可能包括寒热、咳嗽、呼吸困难、嗅觉丧失、味觉缺失、咽痛。最严重的并发症是急性呼吸窘迫综合征和多器官衰竭。临床表现还包括心脏结构（主要是心肌）的急性受损。据报道，约有20%的住院病人的特异性肌钙蛋白水平升高[1]。然而，这并不总是与心肌损伤的其他迹象相关。另一项研究中，对COVID-19患者住院后24小时内的肌钙蛋白I水平进行了检查。发现了36%的病例肌钙蛋白I水平升高。并且，即使是很小的心肌病损体积也会导致死亡率显著增加[2]。然而，COVID-19中心肌损伤的许多方面仍不清楚。

发病机制和临床表现

详细了解心脏受损的发病机制是一个至关重要的问题。这样才能及时治疗，避免严重后果，包括死亡。

迄今为止，SARS-CoV-2可渗透到心肌细胞并对其造成直接受损的理论越来越少得到证实。在

COVID-19患者中经常可以观察到伴发的淋巴细胞性心肌炎。但它的发生被归因于由细胞因子介导的全身炎症反应。一些研究[3-5]中，心肌活检显示了淋巴细胞浸润、间质水肿和局限性坏死病灶。但未发现细胞内病毒物质。D.Lindner等人[3]研究了COVID-19患者的尸检材料。这些患者没有暴发性心肌炎的临床表现。D.Lindner等人描述了COVID-19病原体在心肌中的存在。但COVID-19病原体主要不是存在于心肌细胞中，而是存在于浸润心肌组织的间质细胞和巨噬细胞中。病毒的存在与心肌增强单核浸润无关。没有发现心肌炎的组织学迹象（没有大量细胞浸润物或坏死区域的记录）[6]。其他作者也描述了类似的数据[7, 8]。S. E. Fox等人[9]研究了10名死于COVID-19的非裔美国人的尸检结果。在他们的心肌中发现了单个细胞坏死，但没有发现明显的淋巴细胞性心肌炎。没有发现大面积的心肌细胞坏死。这表明了，心脏巨噬细胞中的病毒颗粒存在是病毒血症阶段或浸润的肺泡巨噬细胞向肺外组织迁移的结果。还有人指出，在炎症性心肌损伤（COVID-19患者尸检）的成因中，不能忽视药物治疗的潜在心脏毒性[10]。

病毒直接渗入心脏内皮细胞是心脏受损的另一种潜在机制。内皮受损会导致微血管功能失调，血管稳态转向血管收缩。这会导致器官和组织缺血、炎症和水肿以及血栓形成。SARS-CoV-2通过血管紧张素转换酶2型（ACE2）受体穿透内皮细胞，引起活跃的炎症。一些作者描述了弥漫性血管炎。SARS-CoV-2被认为是弥漫性血管炎的直接病因。据推测，由于微血管功能失调，内皮炎可能会引起具有COVID-19特征的多器官功能失调[11]。但这些数据仍然很少，需要进一步证实。

另一种观点认为，心脏受损可能是由于免疫系统过度激活，释放多种炎症介质造成的。“细胞因子风暴”一词经常被用来描述这种受损。由于血小板、中性粒细胞和炎症反应的其他成分激活，微循环和大循环通道的血管中出现血栓。这会导致血管闭塞和细胞死亡。COVID-19的血栓形成常见于动脉和静脉通道[12]。在一项观察性研究中，与没有发生心肌梗死的COVID-19患者相比，COVID-19和ST段抬高型心肌梗死患者的肌钙蛋白水平更高，血栓形成也更多[13]。没有冠状动脉闭塞迹象的急性冠状动脉综合征病例也很常见。因此，S. Bangalore等人的研究[14]中，对18例COVID-19和心电图ST段抬高的患者进行了研究。44%的患者被诊断为导致心肌梗死的急性冠状动脉血栓形成。56%的病例种发现了非冠状动脉心肌损伤。心肌炎的非特异性症状以及乏力、呼吸困难、心动过速和胸部不舒服等表现导致诊断困难。

在冠状病毒感染引起的炎性心肌损伤中，尤其值得注意的是暴发性心肌炎。在暴发性心肌炎中，左心室的收缩功能会迅速下降。通常，这种情况是在双侧肺受损的背景下发生的。可能发生心包积液，甚至导致心脏填塞。约有三分之一的

患者中会发生心源性休克。死亡率约为26%。据报道,接种冠状病毒感染疫苗后曾出现过单例暴发性心肌炎病例。但接种疫苗后,该病的病程较轻。研究表明了,罹患暴发性心肌炎的可能性并不取决于冠状病毒感染或接种疫苗,而主要取决于是否存在易感性[15]。

心律失常是心脏受损最危险的临床表现之一。这种疾病的实际发生率仍然未知。但有证据表明,在44.4%的病例中,心律失常是病人转入重症监护室的原因[16]。COVID-19中的心律失常可能是电解质失衡的结果,可能是原有心律失常的表现,也可能是心肌炎引起的[17]。各类病例所占的比例很难确定。根据G. Peretto等人数据[18],在78.7%的确诊心肌炎患者中观察到一种或另一种形式的心室节律紊乱。我们有理由相信,心律失常的病理生理学还取决于心肌损伤的阶段,因为急性心肌炎和已治愈的心肌炎患者的心律失常特征各不相同。

COVID-19导致心律失常的可能机制包括:心肌细胞直接受损,质膜完整性和电导率受到破坏;心包感染和大量水肿;周细胞感染导致的微血管病变引起的缺血;心肌纤维化导致的心律失常;促炎细胞因子的作用[19, 20]。后一种机制的基础是炎细胞因子,尤其是白细胞介素-6 (IL-6),使桥粒蛋白盘状球蛋白从心肌细胞膜上移位[21]。这可能会导致心律失常,因为人们认为,在细胞间的粘附力不足的情况下,会破坏细胞膜,并导致细胞死亡和随后的纤维化。桥粒蛋白表面表达减少被认为是心律失常性心肌病的主要机制之一[22]。有证据表明,COVID-19患者的血清IL-6浓度升高[23]。IL-6水平与患者病情的严重程度相关。因此,COVID-19可能会导致患者的心律紊乱。尤其是当患者有遗传倾向时。值得强调的是,前三种情况可能是在活动性心肌炎的情况下发生的。而后两种情况则可能发生在慢性或已治愈的心肌炎患者身上。

重要的是,冠状病毒感染易导致一组职业运动员患上心肌炎。这一点已被研究证实。反过来,心肌炎在运动员心脏性猝死的发病机制中也起着重要作用。运动负荷可能会引发危及生命的心律紊乱。运动负荷对免疫功能有影响。中等强度的运动可以改善免疫反应。相反,剧烈运动则会大大降低免疫反应[24]。急性心肌炎患者猝死的原因是心脏肌肉内膜受损。受影响的心肌是导致室性心律失常的基质。在慢性心肌炎中,心肌纤维化会在邻近区域形成re-entry点,从而导致室性心律失常。因此,现代指南建议在确诊心肌炎后的3到6个月内限制体力活动[25]。

冠状病毒感染后心肌梗死的病例已有描述。这种并发症的发生有几种可能的机制,包括病毒包膜糖蛋白与卟啉和血红蛋白 β 链结合,导致缺氧,进而因心肌需氧量和供氧量失衡而引起2型心肌梗死。也有人认为,与冠状病毒感染相关的促血栓形成状态也是心肌梗死的发病机理之一,这可能会导致与动脉粥样硬化斑块不稳定相关的

1型心肌梗死的发生[26]。尽管如此,有证据表明,与其他病因导致的重症肺炎住院患者相比,冠状病毒感染患者的易栓症水平较高,这表明其他机制也可能起作用[27]。

心力衰竭的发生通常是冠状病毒感染导致心脏受损的结果。可能的原因包括病毒对心肌的直接受损、炎性病变、供氧和需氧之间的失衡,以及斑块不稳定导致的动脉粥样硬化血栓形成增加。如果患者原有心脏病,临床表现会更严重,死亡率也会更高[28]。

在冠状病毒感染的罕见心脏表现中,心碎综合征的病例已被描述:肌钙蛋白、NT-proBNP (脑钠肽素) 升高,心电图出现T波倒置和ST段抬高,成像技术显示心肌中段和心尖出现气囊。重要的是,诱发Takotsubo心肌病的因素通常是导致儿茶酚胺释放的精神压力,这在大流行的情况下并不少见[17]。

图1总结了心脏结构受损的主要机制及其引起的临床表现。

诊断心肌炎, 包括COVID-19相关的心肌炎

在临床实践中,心肌炎的诊断是一项复杂的任务。2013年,欧洲心脏病学会(European Society of Cardiology, ESC)心肌和心包疾病工作组确定了心肌炎的推定和明确诊断标准。疑似心肌炎取决于临床表现(心脏部位疼痛)、心电图数据(ST段抬高)、实验室数据(如肌钙蛋白水平升高)和成像技术(超声心动图和磁共振成像(MRI)) [29]。俄罗斯心肌炎诊断临床指南也强调了后者的有效性[30]。

根据Lake Louise标准,磁共振成像是诊断心肌炎的重要方法。这些标准最初发布于2009年。当时的标准包括评估T2加权像(T2-WI)和短T1反转恢复序列上的信号高强度、非冠状动脉型造影剂的延迟聚集[31]。由于对上述特征进行定性评估的主观性,限制了使用原始Lake Louise标准的有效性,因此,2018年对该标准进行了修订,并辅以参数成像技术。这种成像技术允许对心肌T1和T2的区域和整体松弛时间以及细胞外容积(extracellular volume, ECV)进行定量估计。2018年的Lake Louise标准具有更高的灵敏度和特异性(分别为88%和96%) [32]。如果以下两类中每一类至少有一项标准存在,则可在MRI上确认心脏结构的炎性病变: T2-WI上的心肌水肿迹象(T2-WI上的心肌高密度或高T2值) [33]和T1-WI上的心肌损伤迹象(非缺血性延迟增强模式或高T1和/或ECV值) [34]。在只有一种标记物的情况下,如果有适当的临床和/或实验室表现,仍可考虑诊断为心肌炎性病变。然而,在这种情况下磁共振成像的特异性较低。额外的(但不是必须的)迹象是收缩功能障碍(表现为运动功能减退或动作不能)和心包炎迹象(表现为心包叶增强)。要记住,只有在临床怀疑有炎症心脏受损的情况下才可以使用这些标准,而不能将其作为无症状人群的筛查技术。此外,磁共振成像允许

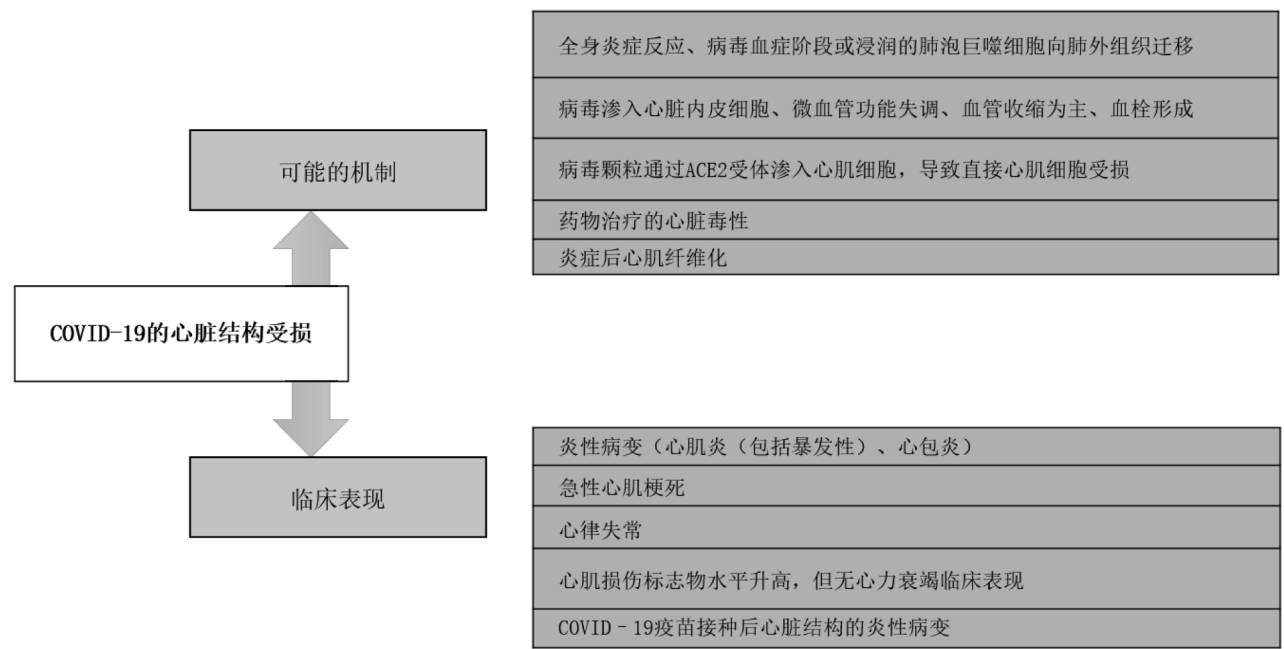


图1。冠状病毒导致的心脏结构受损的主要机制及其引起的临床表现。

发现伴有心肌炎的重要因素，如心肌病的迹象。这些合并症可能会使患者的预后恶化[35]。

诊断的一个重要方面是需要排除冠状动脉损伤。当临床表现不能排除冠状动脉疾病时，这一点尤为重要[36]。不过，即使排除了冠状动脉损伤，我们也不能明确指出临床症状是由心肌炎引起的。此外，还有许多非冠心病心肌损害的类型。患者的病情通常需要进行心内膜心肌活检。这也有助于确定病变的病因。但是，对于没有心力衰竭和/或心律失常威胁的患者来说，很少进行活检。活检是一项侵入性检查。活检过程中会面临许多挑战。根据美国心脏协会（American Heart Association, AHA）目前的临床指南，对于首次出现心力衰竭且血流动力学不稳定的患者来说，必须进行活组织检查，以排除巨细胞或嗜酸性粒细胞浸润的存在，这种病变需要特殊治疗；如果不进行治疗，预后通常不佳[37]。

根据达拉斯标准（Dallas, 1985年），心脏活检和尸检获得的心肌炎组织学数据被定义为心肌中与非缺血性心肌细胞变性或坏死相关的炎症浸润的组织学证据[38]。如果有淋巴细胞浸润且无坏死，则为活动性心肌炎。然而，在病毒性心肌炎的病例中，达拉斯标准并不总是有效：平均而言，在50%已证实存在病原体的此类病例中，心肌炎的标准并不存在[39]。最近，免疫组化特征也被纳入达拉斯标准。免疫组化特征允许将异常炎症浸润的存在考虑在内[36]。此外，还必须存在非缺血性心肌细胞变性和坏死的迹象。

在没有心肌细胞坏死的情况下，正常心肌也可能出现炎症浸润[40]。心肌炎主要由炎症浸润的性质（炎症细胞在肌细胞周围聚集，淋巴细胞多于巨噬细胞）和心肌坏死的存在决定。根据最

近的文献数据，将心肌炎分为感染性（存在实验室确证的病原体）和非感染性（不存在实验室确证的病原体）是有道理的。由于非感染性心肌炎的存在，人们对是否使用心肌活检来诊断心肌炎提出了质疑。目前，这种诊断方法不用于诊断心肌炎，包括与COVID-19相关的心肌炎；诊断的依据是间接征象，如超声心动图或磁共振成像的异常[41]。

一般来说，COVID-19的心肌炎诊断标准保持不变。不过，诊断的途径可能与其他病因引起的心肌炎有所不同。这主要是由于需要保护医护人员免受感染。

与COVID-19相关的心肌炎的诊断可能是通过一些实验室指标来确定的：通常可发现淋巴细胞减少（多达83%的病例），在侵袭性较强的病例中，炎症指标值（D-二聚体、铁蛋白、C反应蛋白）会升高[42]。肌钙蛋白水平升高表明可能的心肌损伤，并可能预示急性心肌炎。肌钙蛋白浓度高，同时炎症指标水平升高，表明存在高炎症状态和多器官功能衰竭[43]。此外，NT-proBNP水平升高可能预示着血流动力学负荷过重[44]。

心肌损伤的心电图指标物并不是心肌炎的病理标志：从窦性心动过速到ST段抬高和T波倒置等各种模式都有描述[44]。

无论是病情稳定还是不稳定的患者，如果临床怀疑患有心肌炎，超声心动图检查是首选的成像技术；但是，该方法在诊断心肌炎方面也有局限性：例如，心室功能失调可能由多种其他缺血性或非缺血性病因引起，并非心肌炎的特定症状；左心室分数正常也不能排除心肌炎的存在[45]。

一般来说，心肌肌钙蛋白水平升高可定义为心脏受损：文献报道，COVID-19患者中有18-28%出

现这种情况[28]。如上所述, COVID-19患者中很少发现心肌炎。一项对因COVID-19而死亡的患者心肌尸检的277份报告(22项研究)的大型综述显示了, 此类病例约占7.8%。然而, 与该疾病相关的其他组织病理学也是已知的: 12.6%的病例中发现了无心肌炎症状的炎症浸润, 13.7%的病例中发现了单个心肌细胞缺血性损伤, 4.7%的病例中发现了急性心肌梗死[46]。尸检时心肌炎的发生率较低, 这与文献中COVID-19康复患者磁共振成像心肌炎的发生率约60%形成鲜明对比。在一项对15名具有特征性症状的 COVID-19康复患者的研究中, 58%的病例在磁共振成像扫描中显示出心肌损伤(水肿、纤维化、心室功能失调)的迹象[47]。另一项设计类似的研究显示了, 78%的康复者在磁共振成像中发现心肌损伤迹象, 75%的病例肌钙蛋白水平升高[48]。这些研究表明了, 即使在康复一段时间后, 心脏受损并随后心室功能失调的风险依然存在。

目前, 心脏磁共振成像并不总能提供心肌炎的信息, 因为该方法的分辨率在这方面存在局限性。由于无法发现心肌细胞中的病毒, 因此不建议进行心肌活检。在这种情况下, 科学家们正在积极寻找诊断心肌炎的新方法。其中之一就是发现辅助性T细胞17产生的微小核糖核酸(microRNA)的方法。它们是急性期心肌损伤的积极参与者, 也是心肌炎和扩张型心肌病发展的结果因素。研究人员在小鼠模型上(使用了实验性自身免疫性心肌炎和病毒性心肌炎)已经发现了一种作为心肌炎标志物的新microRNA及其人类同源物。确定的是, 使用这种标记物可以区分心肌炎和心肌梗塞。然而, 问题仍然多于答案。例如, 目前还不清楚如何解释这种microRNA水平的更大变异性, 以及它是否反映患者病情的严重程度; 它是否能区分心肌炎和扩张型心肌病等病症[49]。在这一方面上的进一步研究将使我们能够开发出一种无创诊断心肌炎的技术。

要考虑到, 在以前的冠状病毒变种引起的流行病中, 要么没有发现心肌炎病例(在SARS中), 要么被分离出来(在MERS中)[50, 51]。由于心肌细胞表面ACE2受体表达有限, COVID-19病原体对心肌细胞的嗜性程度平均较低。这些数据和其他数据表明, COVID-19导致心肌损伤的直接原因可能是内皮细胞活化、细胞因子风暴、电解质失衡和其他可能的免疫机制[46]。此外, 还应考虑到, 如果心电图异常、肌钙蛋白阳性而冠状动脉正常, 则心碎综合征可能是心肌损伤的潜在原因之一[52]。还应将心肌炎与败血症相关心肌病和急性冠状动脉综合征(尤其是暴发性心肌炎)等疾病进行鉴别诊断。

COVID-19疫苗接种引起的心肌炎

由于目前还没有针对COVID-19的病因治疗方法, 疫苗接种仍是控制大流行的主要手段; 有

效的疫苗可显著降低死亡率。迄今为止, 全球公认的疫苗有: AstraZeneca/Oxford、Johnson and Johnson、Moderna、Pfizer/BioNTech、Sinopharm、Sinovac、Sputnik V。目前已开发出几种疫苗开发原则, 包括基于RNA和DNA的制剂(一种使用转基因RNA或DNA来产生可引起免疫反应的蛋白的方法)和基于运载体的制剂(使用一种不会致病但可作为产生冠状病毒蛋白质平台的安全病毒, 以引起免疫反应); 灭活疫苗(使用一种弱化的病毒来产生免疫反应); 基于蛋白的疫苗(使用模拟COVID-19病原体的安全蛋白或蛋白片段, 以产生免疫反应)。通过非复制重组腺病毒载体系统递送的DNA是 AstraZeneca/Oxford、Johnson and Johnson和Sputnik V疫苗的基础。Moderna和Pfizer/BioNTech疫苗的基础是mRNA技术和脂质纳米颗粒递送系统[53-56]。与基于mRNA的疫苗一样, 基于运载体的疫苗可刺激S蛋白SARS-CoV-2的产生, 而S蛋白是自然感染或接种疫苗产生的中和抗体的主要靶标。

在接种计划过程中, 偶尔会有文献报道疫苗的副作用。据认为, 在某些情况下, 这些反应可能会导致血小板聚集增强、血栓形成和炎症。一种潜在的机制可能是疫苗所针对的体细胞形成了游离循环的刺突蛋白, 这些蛋白能够与ACE2受体相互作用[57]。

据报道, 接种COVID-19疫苗后(大多发生在6小时至4天后)出现了心肌炎和心包炎病例[58, 59], 主要发生在接种基于mRNA的疫苗(Pfizer和Moderna)的人群中。以色列对接种Pfizer疫苗的人群进行了两项大型回顾性研究。其中一项研究在510多万名参与者中发现了136例心肌炎病例(第一剂疫苗接种21天后, 第二剂疫苗接种30天后); 95%的病例症状轻微, 一例病例死亡[60]。研究指出了, 这些症状最常发生在年轻男性身上。另一项同样在以色列进行的研究检查了250多万Pfizer疫苗接种者的记录, 发现心肌炎的发病率为十万分之2.3, 其中16至29岁的年轻男性发病率为十万分之10[61]。还有证据表明, COVID-19病原体感染者患心肌炎的总风险度是未感染者的18.28倍, 即患心肌炎的风险明显高于接种疫苗后(平均是未接种者的3.24倍)[62]。尽管上述所有研究中的心肌炎症状都出现在接种疫苗的时间附近, 且作者排除了其他可能的原因(即接种疫苗被认为是心肌炎的原因), 但这一现象的病理生理学仍不完全清楚。现有的假说认为这可能是由于非特异性炎症反应或分子模拟引起的抗体交叉反应所致, 这与患者在接受抗炎治疗后病情好转的事实相关[58]。

结论

COVID-19可导致很高的死亡率, 包括伴有心脏病的患者。然而, 人们对其发病机制仍知之甚

少。与SARS-CoV-2相关的心肌炎被认为是主要原因。然而，根据文献，在确诊冠状病毒感染患者的组织学研究中很少看到心肌炎性病变。病毒本身是很少在心脏组织中发现的，不是集中在心肌细胞中，而是集中在免疫细胞中。在心肌中发现的大多是非特异性炎症浸润。考虑到这些事实，心内膜心肌活检似乎不应被广泛用于COVID-19的心肌炎诊断。

接种疫苗（主要是基于mRNA的疫苗）也可能导致心肌炎性病变。这种并发症在年轻人中更为常见。大多数情况下症状较轻。疫苗接种导致心肌炎的这种发病率并不能成为避免接种疫苗的合理理由，对年轻人也是如此。

СПИСОК ЛИТЕРАТУРЫ

1. Shi S., Qin M., Shen B., et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China // *JAMA Cardiol.* 2020. Vol. 5, N 7. P. 802–810. doi: 10.1001/jamacardio.2020.0950
2. Lala A., Johnson K.W., Januzzi J.L., et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection // *J Am Coll Cardiol.* 2020. Vol. 76, N 5. P. 533–546. doi: 10.1016/j.jacc.2020.06.007
3. Lindner D., Fitzek A., Bräuninger H., et al. Association of cardiac infection with SARS-CoV-2 in confirmed COVID-19 autopsy cases // *JAMA Cardiol.* 2020. Vol. 5, N 11. P. 1–5. doi: 10.1001/jamacardio.2020.3551
4. Sala S., Peretto G., Gramegna M., et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection // *Eur Heart J.* 2020. Vol. 41, N 19. P. 1861–1862. doi: 10.1093/eurheartj/ehaa286
5. Escher F., Pietsch G., Aleshcheva G., et al. Detection of viral SARS-CoV-2 genomes and histopathological changes in endomyocardial biopsies // *ESC Heart Fail.* 2020. Vol. 7, N 5. P. 2440–2447. doi: 10.1002/ehf2.12805
6. Tavazzi G., Pellegrini C., Maurelli M., et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock // *Eur J Heart Fail.* 2020. Vol. 22, N 5. P. 911–915. doi: 10.1002/ehf.1828
7. Wichmann D. Autopsy findings and venous thromboembolism in patients with COVID-19 // *Ann Intern Med.* 2020. Vol. 173, N 12. P. 1030. doi: 10.7326/L20-1206
8. Buja L.M., Wolf D.A., Zhao B., et al. The emerging spectrum of cardiopulmonary pathology of the coronavirus disease 2019 (COVID-19): Report of 3 autopsies from Houston, Texas, and review of autopsy findings from other United States cities // *Cardiovasc Pathol.* 2020. N 48. P. 107233. doi: 10.1016/j.carpath.2020.107233
9. Fox S.E., Akmatbekov A., Harbert J.L., et al. Pulmonary and cardiac pathology in African American patients with COVID-19: An autopsy series from New Orleans // *Lancet Respir Med.* 2020. Vol. 8, N 7. P. 681–686. doi: 10.1016/S2213-2600(20)30243-5
10. Alijotas-Reig J., Esteve-Valverde E., Belizna C., et al. Immunomodulatory therapy for the management of severe COVID-19. Beyond the anti-viral therapy: A comprehensive review // *Autoimmun Rev.* 2020. Vol. 19, N 7. P. 102569. doi: 10.1016/j.autrev.2020.102569
11. Varga Z., Flammer A.J., Steiger P., et al. Endothelial cell infection and endotheliitis in COVID-19 // *Lancet Lond Engl.* 2020. Vol. 395, N 10234. P. 1417–1418. doi: 10.1016/S0140-6736(20)30937-5
12. Bikdeli B., Madhavan M.V., Jimenez D., et al. COVID-19 and thrombotic or thromboembolic disease: Implications for prevention,

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antithrombotic therapy, and follow-up: JACC state-of-the-art review // *J Am Coll Cardiol.* 2020. Vol. 75, N 23. P. 2950–2973. doi: 10.1016/j.jacc.2020.04.031

13. Choudry F.A., Hamsheer S.M., Rathod K.S., et al. High thrombus burden in patients with COVID-19 presenting with ST-segment elevation myocardial infarction // *J Am Coll Cardiol.* 2020. Vol. 76, N 10. P. 1168–1176. doi: 10.1016/j.jacc.2020.07.022

14. Bangalore S., Sharma D., Slotwimer A., et al. ST-Segment elevation in patients with Covid-19: A case series // *N Engl J Med.* 2020. Vol. 382, N 25. P. 2478–2480. doi: 10.1056/NEJMc2009020

15. Guglin M.E., Etuk A., Shah C., et al. Fulminant myocarditis and cardiogenic shock following COVID-19 infection versus COVID-19 vaccination: A systematic literature review // *J Clin Med.* 2023. Vol. 12, N 5. P. 1849. doi: 10.3390/jcm12051849

16. Wang D., Hu B., Hu C., et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China // *JAMA.* 2020. Vol. 323, N 11. P. 1061–1069. doi: 10.1001/jama.2020.1585

17. Siripanthong B., Nazarian S., Muser D., et al. Recognizing COVID-19-related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management // *Heart Rhythm.* 2020. Vol. 17, N 9. P. 1463–1471. doi: 10.1016/j.hrthm.2020.05.001

18. Peretto G., Sala S., Rizzo S., et al. Ventricular arrhythmias in myocarditis: Characterization and relationships with myocardial inflammation // *J Am Coll Cardiol.* 2020. Vol. 75, N 9. P. 1046–1057. doi: 10.1016/j.jacc.2020.01.036

19. Peretto G., Sala S., Rizzo S., et al. Arrhythmias in myocarditis: State of the art // *Heart Rhythm.* 2019. Vol. 16, N 5. P. 793–801. doi: 10.1016/j.hrthm.2018.11.024

20. Chen L., Li X., Chen M., et al. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2 // *Cardiovasc Res.* 2020. Vol. 116, N 6. P. 1097–1100P. doi: 10.1093/cvr/cvaa078

21. Asimaki A., Tandri H., Duffi E.R., et al. Altered desmosomal proteins in granulomatous myocarditis and potential pathogenic links to arrhythmogenic right ventricular cardiomyopathy // *Circ Arrhythm Electrophysiol.* 2011. Vol. 4, N 5. P. 743–752. doi: 10.1161/CIRCEP.111.964890

22. Gemayel C., Pelliccia A., Thompson P.D. Arrhythmogenic right ventricular cardiomyopathy // *J Am Coll Cardiol.* 2001. Vol. 38, N 7. P. 1773–1781. doi: 10.1016/s0735-1097(01)01654-0

23. Coomes E.A., Haghighbayan H. Interleukin-6 in Covid-19: A systematic review and meta-analysis // *Rev Med Virol.* 2020. Vol. 30, N 6. P. 1–9. doi: 10.1002/rmv.2141
24. Modica G., Bianco M., Sollazzo F., et al. Myocarditis in athletes recovering from COVID-19: A systematic review and meta-analysis // *Int J Environ Res Public Health.* 2022. Vol. 19, N 7. P. 4279. doi: 10.3390/ijerph19074279
25. Eichhorn C., Biere L., Schnell F., et al. Myocarditis in athletes is a challenge: Diagnosis, risk stratification, and uncertainties // *JACC Cardiovasc Imaging.* 2020. Vol. 13, N 2, Pt. 1. P. 494–507. doi: 10.1016/j.jcmg.2019.01.039
26. Azevedo R.B., Botelho B.G., de Hollanda G., et al. Covid-19 and the cardiovascular system: A comprehensive review: 1 // *J Hum Hypertens.* 2021. Vol. 35, N 1. P. 4–11. doi: 10.1038/s41371-020-0387-4
27. Klok F.A., Kruip M.J., van der Meer H.J., et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19 // *Thromb Res.* 2020. N 191. P. 145–147. doi: 10.1016/j.thromres.2020.04.013
28. Guo T., Fan Y., Chen M., et al. Cardiovascular Implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19) // *JAMA Cardiol.* 2020. Vol. 5, N 7. P. 811–818. doi: 10.1001/jamacardio.2020.1017
29. Ларина О.М. Магнитно-резонансная томография сердца в диагностике острого миокардита: клинический случай и обзор литературы // *Вестник рентгенологии и радиологии.* 2014. № 5. С. 54–59.
30. Арутюнов Г.Б., Палеев Ф.Н., Моисеева О.М. Миокардиты у взрослых. Клинические рекомендации 2020 // *Российский кардиологический журнал.* 2021. Т. 26, № 11. С. 47–90. doi: 10.15829/1560-4071-2021-4790
31. Friedrich M.G., Sechtem U., Schulz-Menger J., et al. Cardiovascular magnetic resonance in myocarditis: A JACC white paper // *J Am Coll Cardiol.* 2009. Vol. 53, N 17. P. 1475–1487. doi: 10.1016/j.jacc.2009.02.007
32. Tijmes S.F., Thavendiranathan P., Udell J.A., et al. Cardiac MRI assessment of nonischemic myocardial inflammation: State of the art review and update on myocarditis associated with COVID-19 vaccination // *Radiol Cardiothorac Imaging.* 2021. Vol. 3, N 6. P. e210252. doi: 10.1148/ryct.210252
33. Srichai M.B., Lim R.P., Lath N., et al. Diagnostic performance of dark-blood T2-weighted CMR for evaluation of acute myocardial injury // *Invest Radiol.* 2013. Vol. 48, N 1. P. 24–31. doi: 10.1097/RLI.0b013e3182718672
34. Galán-Arriola C., Lobo M., Vilchez-Tschischke J.P., et al. Serial magnetic resonance imaging to identify early stages of anthracycline-induced cardiotoxicity // *J Am Coll Cardiol.* 2019. Vol. 73, N 7. P. 779–791. doi: 10.1016/j.jacc.2018.11.046
35. Благова О.В., Павленко Е.В., Вариончик Н.В., и др. Миокардит как закономерный феномен у больных с первичным некомпактным миокардом: диагностика, лечение и влияние на исходы // *Российский кардиологический журнал.* 2018. N 2. С. 44–52. doi: 10.15829/1560-4071-2018-2-44-52
36. Caforio A.L., Pankuweit S., Arbustini E., et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases // *Eur Heart J.* 2013. Vol. 34, N 33. P. 2636–2648, 2648a–2648d. doi: 10.1093/eurheartj/ehd210
37. Cooper L.T., Baughman K.L., Feldman A.M., et al. The role of endomyocardial biopsy in the management of cardiovascular disease: A scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology // *Circulation.* 2007. Vol. 116, N 19. P. 2216–2233. doi: 10.1161/CIRCULATIONAHA.107.186093
38. Aretz H.T. Myocarditis: The Dallas criteria // *Hum Pathol.* 1987. Vol. 18, N 6. P. 619–624. doi: 10.1016/s0046-8177(87)80363-5
39. Dennert R., Crijns H.J., Heymans S. Acute viral myocarditis // *Eur Heart J.* 2008. Vol. 29, N 17. P. 2073–2082. doi: 10.1093/eurheartj/ehn296
40. Zhang M., Tavora F., Zhang Y., et al. The role of focal myocardial inflammation in sudden unexpected cardiac and noncardiac deaths: A clinicopathological study // *Int J Legal Med.* 2013. Vol. 127, N 1. P. 131–138. doi: 10.1007/s00414-011-0634-x
41. Титов В.А., Игнатъева В.С., Митрофанова Л.Б. Сравнительное исследование информативности неинвазивных методов диагностики воспалительных заболеваний миокарда // *Российский кардиологический журнал.* 2018. Т. 23, N 2. С. 53–59.
42. Zhou F., Yu T., Fan R., et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study // *Lancet Lond Engl.* 2020. Vol. 395, N 10229. P. 10541062. doi: 10.1016/S0140-6736(20)30566-3
43. Mehta P., McAuley D.F., Brown M., et al. COVID-19: Consider cytokine storm syndromes and immunosuppression // *Lancet Lond Engl.* 2020. Vol. 395, N 10229. P. 1033–1034. doi: 10.1016/S0140-6736(20)30628-0
44. Castiello T., Georgiopoulos G., Finocchiaro G., et al. COVID-19 and myocarditis: A systematic review and overview of current challenges // *Heart Fail Rev.* 2022. Vol. 27, N 1. P. 251–261. doi: 10.1007/s10741-021-10087-9
45. Mele D., Flamigni F., Rapezzi C., et al. Myocarditis in COVID-19 patients: Current problems // *Intern Emerg Med.* 2021. Vol. 16, N 5. P. 1123–1129. doi: 10.1007/s11739-021-02635-w
46. Halushka M.K., Vander Heide R.S. Myocarditis is rare in COVID-19 autopsies: Cardiovascular findings across 277 postmortem examinations // *Cardiovasc Pathol.* 2021. N 50. P. 107300. doi: 10.1016/j.carpath.2020.107300
47. Huang L., Zhao P., Tang D., et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging // *JACC Cardiovasc Imaging.* 2020. Vol. 13, N 11. P. 2330–2339. doi: 10.1016/j.jcmg.2020.05.004
48. Puntmann V.O., Carerj M.L., Wieters I., et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19) // *JAMA Cardiol.* 2020. Vol. 5, N 11. P. 1265–1273. doi: 10.1001/jamacardio.2020.3557
49. Blanco-Domínguez R., Sánchez-Díaz R., de la Fuente H., et al. A novel circulating MicroRNA for the detection of acute myocarditis // *N Engl J Med.* 2021. Vol. 384, N 21. P. 2014–2027. doi: 10.1056/NEJMoa2003608
50. Tan L., Wang Q., Zhang D., et al. Lymphopenia predicts disease severity of COVID-19: A descriptive and predictive study // *Signal Transduct Target Ther.* 2020. Vol. 5, N 1. P. 33. doi: 10.1038/s41392-020-0148-4
51. Xu Z., Shi L., Zhang J., et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome // *Lancet Respir Med.* 2020. Vol. 8, N 4. P. 420–422. doi: 10.1016/S2213-2600(20)30076-X
52. Kawakami R., Sakamoto A., Kawai K., et al. Pathological evidence for SARS-CoV-2 as a cause of myocarditis // *J Am Coll Cardiol.* 2021. Vol. 77, N 3. P. 314–325. doi: 10.1016/j.jacc.2020.11.031

53. Baden L.R., Sahly H.M., Essink B., et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine // *N Engl J Med*. 2021. Vol. 384, N 5. P. 403–416. doi: 10.1056/NEJMoa2035389
54. Logunov D.Y., Dolzhikova I.V., Shcheblyakov D.V., et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: An interim analysis of a randomised controlled phase 3 trial in Russia // *Lancet*. 2021. Vol. 397, N 10275. P. 671–681. doi: 10.1016/S0140-6736(21)00234-8
55. Polack F.P., Thomas S.J., Kitchin N., et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine // *N Engl J Med*. 2020. Vol. 383, N 27. P. 2603–2615. doi: 10.1056/NEJMoa2034577
56. Voysey M., Costa Clemens S.A., Madhi S.A., et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: An interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK // *Lancet*. 2021. Vol. 397, N 10269. P. 99–111. doi: 10.1016/S0140-6736(20)32661-1
57. Shiravi A.A., Ardekani A., Sheikhabaei E., et al. Cardiovascular complications of SARS-CoV-2 vaccines: An overview // *Cardiol Ther*. 2021. Vol. 11, N 1. P. 13–21 doi: 10.1007/s40119-021-00248-0
58. Watad A., De Marco G., Mahajna H., et al. Immune-Mediated disease flares or new-onset disease in 27 subjects following mRNA/DNA SARS-CoV-2 Vaccination: 5 // *Vaccines*. 2021. Vol. 9, N 5. P. 435. doi: 10.3390/vaccines9050435
59. Albert E., Aurigemma G., Saucedo J., et al. Myocarditis following COVID-19 vaccination // *Radiol Case Rep*. 2021. Vol. 16, N 8. P. 2142–2145. doi: 10.1016/j.radcr.2021.05.033
60. Mevorach D., Anis E., Cedar N., et al. Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel // *N Engl J Med*. 2021. Vol. 385, N 23. P. 2140–2149. doi: 10.1056/NEJMoa2109730
61. Witberg G., Barda N., Hoss S., et al. Myocarditis after Covid-19 vaccination in a large health care organization // *N Engl J Med*. 2021. Vol. 385, N 23. P. 2132–2139. doi: 10.1056/NEJMoa2110737
62. Barda N., Dagan N., Ben-Shlomo Y., et al. Safety of the BNT162b2 mRNA Covid-19 vaccine in a nationwide setting // *N Engl J Med*. 2021. Vol. 385, N 12. P. 1078–1090. doi: 10.1056/NEJMoa2110475

REFERENCES

1. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020;5(7):802–810. doi: 10.1001/jamacardio.2020.0950
2. Lala A, Johnson KW, Januzzi JL, et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. *J Am Coll Cardiol*. 2020;76(5):533–546. doi: 10.1016/j.jacc.2020.06.007
3. Lindner D, Fitzek A, Bräuninger H, et al. Association of cardiac infection with SARS-CoV-2 in confirmed COVID-19 autopsy cases. *JAMA Cardiol*. 2020;5(11):1–5. doi: 10.1001/jamacardio.2020.3551
4. Sala S, Peretto G, Gramegna M, et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. *Eur Heart J*. 2020;41(19):1861–1862. doi: 10.1093/eurheartj/ehaa286
5. Escher F, Pietsch H, Aleshcheva G, et al. Detection of viral SARS-CoV-2 genomes and histopathological changes in endomyocardial biopsies. *ESC Heart Fail*. 2020;7(5):2440–2447. doi: 10.1002/ehf2.12805
6. Tavazzi G, Pellegrini C, Maurelli M, et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. *Eur J Heart Fail*. 2020;22(5):911–915. doi: 10.1002/ejhf.1828
7. Wichmann D. Autopsy findings and venous thromboembolism in patients with COVID-19. *Ann Intern Med*. 2020;173(12):1030. doi: 10.7326/L20-1206
8. Buja LM, Wolf DA, Zhao B, et al. The emerging spectrum of cardiopulmonary pathology of the coronavirus disease 2019 (COVID-19): Report of 3 autopsies from Houston, Texas, and review of autopsy findings from other United States cities. *Cardiovasc Pathol*. 2020;48(4):107233. doi: 10.1016/j.carpath.2020.107233
9. Fox SE, Akmatbekov A, Harbert JL, et al. Pulmonary and cardiac pathology in African American patients with COVID-19: An autopsy series from New Orleans. *Lancet Respir Med*. 2020;10(7):681–686. doi: 10.1016/S2213-2600(20)30243-5
10. Alijotas-Reig J, Esteve-Valverde E, Belizna C, et al. Immunomodulatory therapy for the management of severe COVID-19. Beyond the anti-viral therapy: A comprehensive review. *Autoimmun Rev*. 2020;19(7):102569. doi: 10.1016/j.autrev.2020.102569
11. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet Lond Engl*. 2020;395(10234):1417–1418. doi: 10.1016/S0140-6736(20)30937-5
12. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: Implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. *J Am Coll Cardiol*. 2020;75(23):2950–2973. doi: 10.1016/j.jacc.2020.04.031
13. Choudry FA, Hamshire SM, Rathod KS, et al. High thrombus burden in patients with Covid-19 presenting with ST-segment elevation myocardial infarction. *J Am Coll Cardiol*. 2020;76(10):1168–1176. doi: 10.1016/j.jacc.2020.07.022
14. Bangalore S, Hamshire SM, Rathod KS, et al. ST-Segment elevation in patients with Covid-19: A case series. *N Engl J Med*. 2020;382(25):2478–2480. doi: 10.1056/NEJMc2009020
15. Guglin ME, Etuk A, Shah C, et al. Fulminant myocarditis and cardiogenic shock following COVID-19 infection versus COVID-19 vaccination: A systematic literature review. *J Clin Med*. 2023;12(5):1849. doi: 10.3390/jcm12051849
16. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–1069. doi: 10.1001/jama.2020.1585
17. Siripanthong B, Nazarian S, Muser D, et al. Recognizing COVID-19-related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm*. 2020;17(9):1463–1471. doi: 10.1016/j.hrthm.2020.05.001
18. Peretto G, Sala S, Rizzo S, et al. Ventricular arrhythmias in myocarditis: Characterization and relationships with myocardial inflammation. *J Am Coll Cardiol*. 2020;75(9):1046–1057. doi: 10.1016/j.jacc.2020.01.036
19. Peretto G, Sala S, Rizzo S, et al. Arrhythmias in myocarditis: State of the art. *Heart Rhythm*. 2019;16(5):793–801. doi: 10.1016/j.hrthm.2018.11.024
20. Chen L, Li X, Chen M, et al. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients

- infected with SARS-CoV-2. *Cardiovasc Res.* 2020;116(6):1097–1100. doi: 10.1093/cvr/cvaa078
21. Asimaki A, Tandri H, Duffy ER, et al. Altered desmosomal proteins in granulomatous myocarditis and potential pathogenic links to arrhythmogenic right ventricular cardiomyopathy. *Circ Arrhythm Electrophysiol.* 2011;4(5):743–752. doi: 10.1161/CIRCEP.111.964890
22. Gemayel C, Pelliccia A, Thompson PD. Arrhythmogenic right ventricular cardiomyopathy. *J Am Coll Cardiol.* 2001;38(7):1773–1781. doi: 10.1016/s0735-1097(01)01654-0
23. Coomes EA, Haghighyan H. Interleukin-6 in Covid-19: A systematic review and meta-analysis. *Rev Med Virol.* 2020;30(6):1–9. doi: 10.1002/rmv.2141
24. Modica G, Bianco M, Sollazzo F, et al. Myocarditis in athletes recovering from COVID-19: A systematic review and meta-analysis. *Int J Environ Res Public Health.* 2022;19(7):4279. doi: 10.3390/ijerph19074279
25. Eichhorn C, Biere L, Schnell F, et al. Myocarditis in athletes is a challenge: Diagnosis, risk stratification, and uncertainties. *JACC Cardiovasc Imaging.* 2020;13(2):494–507. doi: 10.1016/j.jcmg.2019.01.039
26. Azevedo RB, Botelho BG, de Hollanda G, et al. Covid-19 and the cardiovascular system: A comprehensive review. *J Hum Hypertens.* 2021;35(1):4–11. doi: 10.1038/s41371-020-0387-4
27. Klok FA, Kruip MJ, van der Meer HJ, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res.* 2020;(191):145–147. doi: 10.1016/j.thromres.2020.04.013
28. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol.* 2020;5(7):811–818. doi: 10.1001/jamacardio.2020.1017
29. Larina OM. Cardiac magnetic resonance imaging in the diagnosis of acute myocarditis: A clinical case and review of the literature. *Bulletin Radiol Radiol.* 2014;(5):54–59. (In Russ).
30. Arutyunov GB, Paleev FN, Moiseeva OM. Myocarditis in adults. Clinical recommendations 2020. *Russ Cardiol J.* 2021;26(11):4790. (In Russ). doi: 10.15829/1560-4071-2021-4790
31. Friedrich MG, Sechtem U, Schulz-Menger J, et al. Cardiovascular magnetic resonance in myocarditis: A JACC white paper. *J Am Coll Cardiol.* 2009;53(17):1475–1487. doi: 10.1016/j.jacc.2009.02.007
32. Tijmes SF, Thavendiranathan P, Udel J, et al. Cardiac MRI assessment of nonischemic myocardial inflammation: State of the art review and update on myocarditis associated with COVID-19. *Vaccination Radiol Cardiothorac Imaging.* 2021;3(6):e210252. doi: 10.1148/ryct.210252
33. Srichai MB, Lim RP, Lath N, et al. Diagnostic performance of dark-blood T2-weighted CMR for evaluation of acute myocardial injury. *Invest Radiol.* 2013;48(1):24–31. doi: 10.1097/RLI.0b013e3182718672
34. Galán-Arriola C, Lim RP, Lath N, et al. Serial magnetic resonance imaging to identify early stages of anthracycline-induced cardiotoxicity. *J Am Coll Cardiol.* 2019;73(7):779–791. doi: 10.1016/j.jacc.2018.11.046
35. Blagova OV, Pavlenko EV, Varionchik NV, et al. Myocarditis as a natural phenomenon in patients with primary non-compact myocardium: Diagnosis, treatment and impact on outcomes // *Russ J Cardiol.* 2018;(2):44–52. (In Russ). doi: 10.15829/1560-4071-2018-2-44-52
36. Caforio AL, Pankuweit S, Arbustini E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J.* 2013;34(33):2636–2648, 2648a–2648d. doi: 10.1093/eurheartj/ehd210
37. Cooper LT, Baughman KL, Feldman AM, et al. The role of endomyocardial biopsy in the management of cardiovascular disease: A scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology. *Circulation.* 2007;116(19):2216–2233. doi: 10.1161/CIRCULATIONAHA.107.186093
38. Aretz HT. Myocarditis: The Dallas criteria. *Hum Pathol.* 1987;18(6):619–624. doi: 10.1016/s0046-8177(87)80363-5
39. Dennert R, Crijns HJ, Heymans S. Acute viral myocarditis. *Eur Heart J.* 2008;29(17):2073–2082. doi: 10.1093/eurheartj/ehn296
40. Zhang M, Tavora F, Zhang Y, et al. The role of focal myocardial inflammation in sudden unexpected cardiac and noncardiac deaths: A clinicopathological study. *Int J Legal Med.* 2013;127(1):131–138. doi: 10.1007/s00414-011-0634-x
41. Titov VA, Ignatyeva VS, Mitrofanova LB. Comparative study of informativeness of noninvasive methods for diagnosis of myocardial inflammatory diseases. *Russ J Cardiol.* 2018;23(2):53–59. (In Russ).
42. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet Lond Engl.* 2020;395(10229):1054–1062. doi: 10.1016/S0140-6736(20)30566-3
43. Mehta P, McAuley DF, Brown M, et al. COVID-19: Consider cytokine storm syndromes and immunosuppression. *Lancet Lond Engl.* 2020;395(10229):1033–1034. doi: 10.1016/S0140-6736(20)30628-0
44. Castiello T, Georgiopoulos G, Finocchiaro G, et al. COVID-19 and myocarditis: A systematic review and overview of current challenges. *Heart Fail Rev.* 2022;27(1):251–261. doi: 10.1007/s10741-021-10087-9
45. Mele D, Flamigni F, Rapezzi C, et al. Myocarditis in COVID-19 patients: Current problems. *Intern Emerg Med.* 2021;16(5):1123–1129. doi: 10.1007/s11739-021-02635-w
46. Halushka MK, Vander Heide RS. Myocarditis is rare in COVID-19 autopsies: Cardiovascular findings across 277 postmortem examinations. *Cardiovasc Pathol.* 2021;(50):107300. doi: 10.1016/j.carpath.2020.107300
47. Huang L, Zhao P, Tang D, et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. *JACC Cardiovasc Imaging.* 2020;13(11):2330–2339. doi: 10.1016/j.jcmg.2020.05.004
48. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). *JAMA Cardiol.* 2020;5(11):1265–1273. doi: 10.1001/jamacardio.2020.3557
49. Blanco-Domínguez R, Sánchez-Díaz R, de la Fuente H, et al. A novel circulating MicroRNA for the detection of acute myocarditis. *N Engl J Med.* 2021;384(21):2014–2027. doi: 10.1056/NEJMoa2003608
50. Tan L, Wang Q, Zhang D, et al. Lymphopenia predicts disease severity of COVID-19: A descriptive and predictive study. *Signal Transduct Target Ther.* 2020;5(1):33. doi: 10.1038/s41392-020-0148-4
51. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med.* 2020;8(4):420–422. doi: 10.1016/S2213-2600(20)30076-X
52. Kawakami R, Sakamoto A, Kawai K, et al. Pathological evidence for SARS-CoV-2 as a cause of myocarditis. *J Am Coll Cardiol.* 2021;77(3):314–325. doi: 10.1016/j.jacc.2020.11.031
53. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med.* 2021;384(5):403–416. doi: 10.1056/NEJMoa2035389

- 54.** Logunov DY, Dolzhikova IV, Shcheblyakov DV, et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: An interim analysis of a randomised controlled phase 3 trial in Russia. *Lancet*. 2021;397(10275):671–681. doi: 10.1016/S0140-6736(21)00234-8
- 55.** Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med*. 2020;383(27):2603–2615. doi: 10.1056/NEJMoa2034577
- 56.** Voysey M, Clemens SA, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: An interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet*. 2021;397(10269):99–111. doi: 10.1016/S0140-6736(20)32661-1
- 57.** Shiravi AA, Ardekani A, Sheikhabaei E, et al. Cardiovascular complications of SARS-CoV-2 vaccines: An overview. *Cardiol Ther*. 2021;11(1):13–21. doi: 10.1007/s40119-021-00248-0

- 58.** Watad A, De Marco G, Mahajna H, et al. Immune-Mediated disease flares or new-onset disease in 27 subjects following mRNA/DNA SARS-CoV-2 Vaccination: 5. *Vaccines*. 2021;9(5):435. doi: 10.3390/vaccines9050435
- 59.** Albert E, Aurigemma G, Saucedo J, et al. Myocarditis following COVID-19 vaccination. *Radiol Case Rep*. 2021;16(8):2142–2145. doi: 10.1016/j.radcr.2021.05.033
- 60.** Mevorach D, Anis E, Cedar N, et al. Myocarditis after BNT162b2 mRNA vaccine against Covid-19 in Israel. *N Engl J Med*. 2021;385(23):2140–2149. doi: 10.1056/NEJMoa2109730
- 61.** Witberg G, Barda N, Hoss S, et al. Myocarditis after Covid-19 vaccination in a large health care organization. *N Engl J Med*. 2021;385(23):2132–2139. doi: 10.1056/NEJMoa2110737
- 62.** Barda N, Dagan N, Ben-Shlomo Y, et al. Safety of the BNT162b2 mRNA Covid-19 vaccine in a nationwide setting. *N Engl J Med*. 2021;385(12):1078–1090. doi: 10.1056/NEJMoa2110475

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