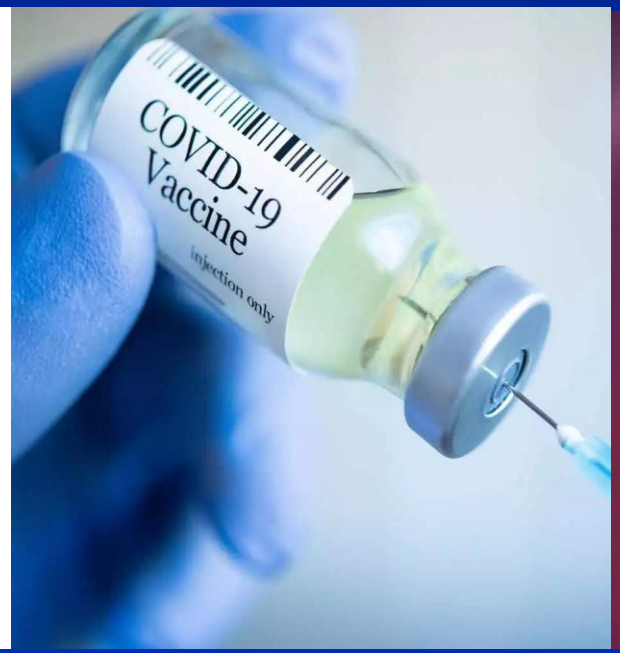
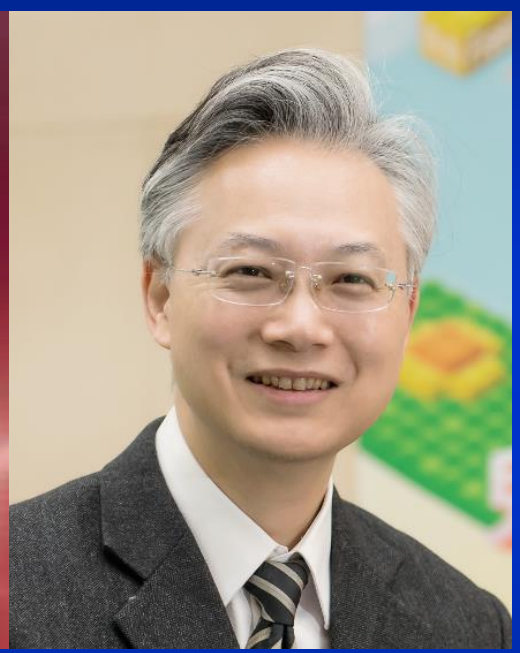
疫苗接種後的心肌炎診斷與處置

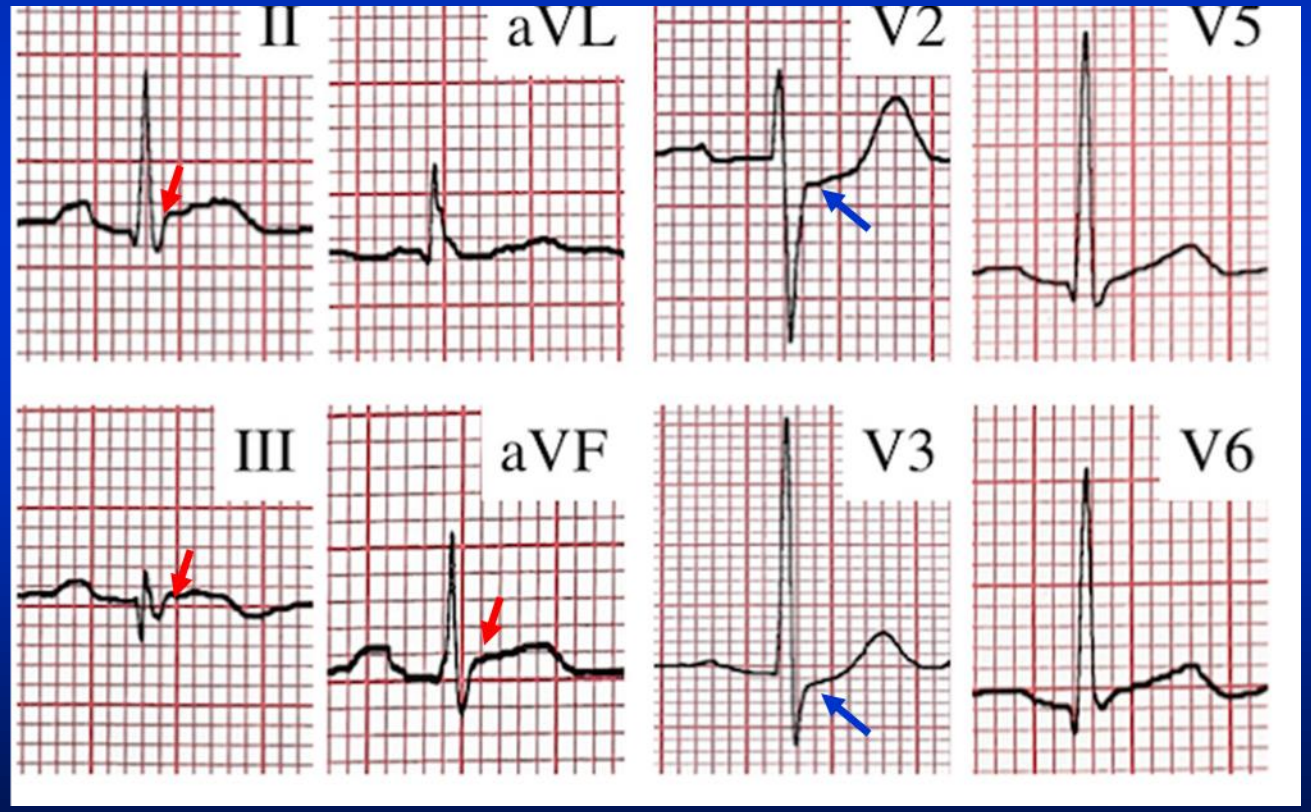




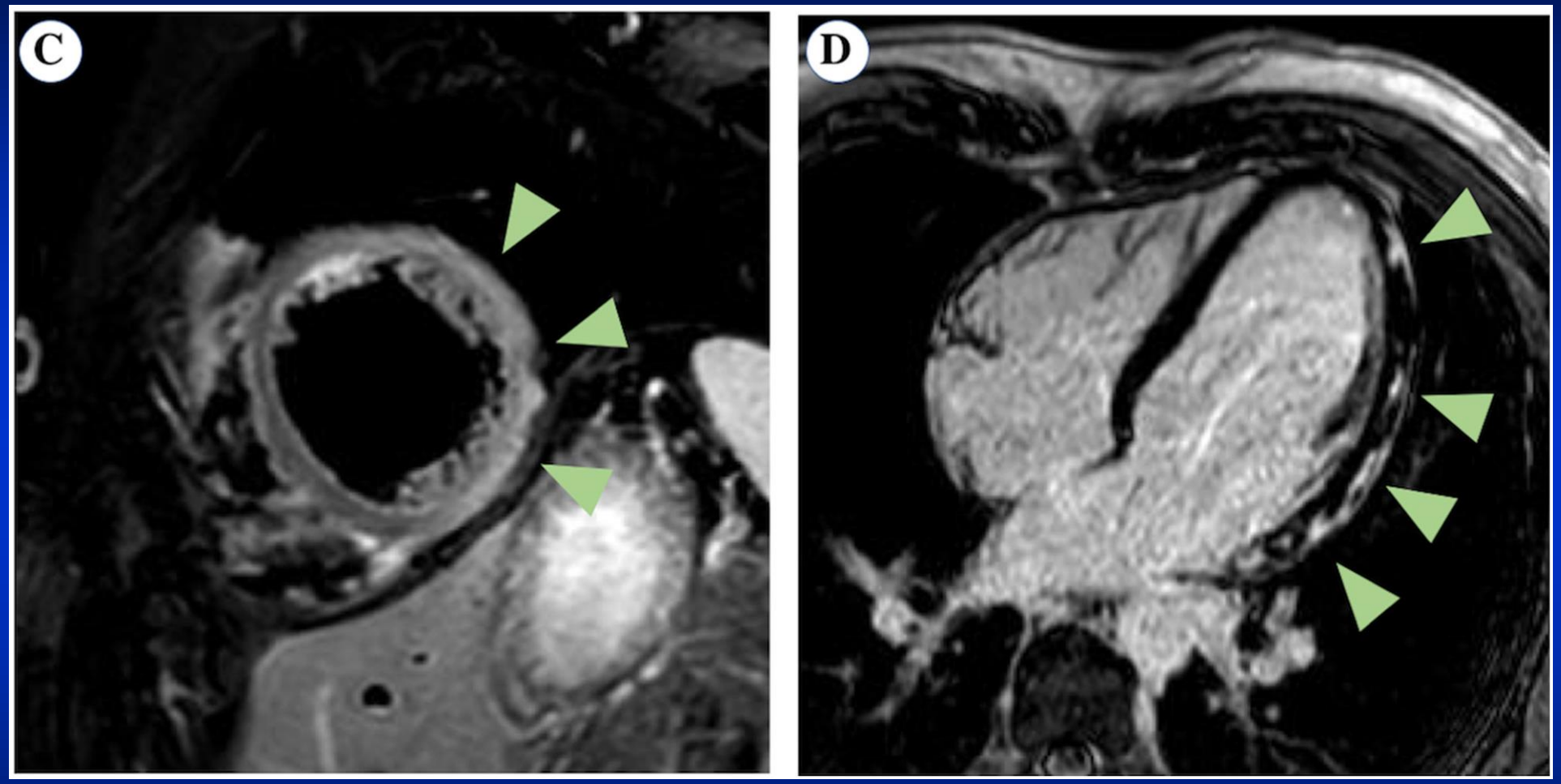
傅雲慶
台中榮民總醫院副院長

Case 1 Rev Port Cardiol. 2021 Jul 24

- 24 y/o female nurse
- BNT 2nd dose
- Chest pain 60 hours later
- Exacerbated by deep breathing
- WBC 9300/ul
- CRP 1.9 mg/dl (<0.5)
- CKMB 79 (<25)
- Troponin-T 1204 ng/l (<14)
- Echocardiogram EF 45%
- Coronary angiogram: normal



Cardiac MRI

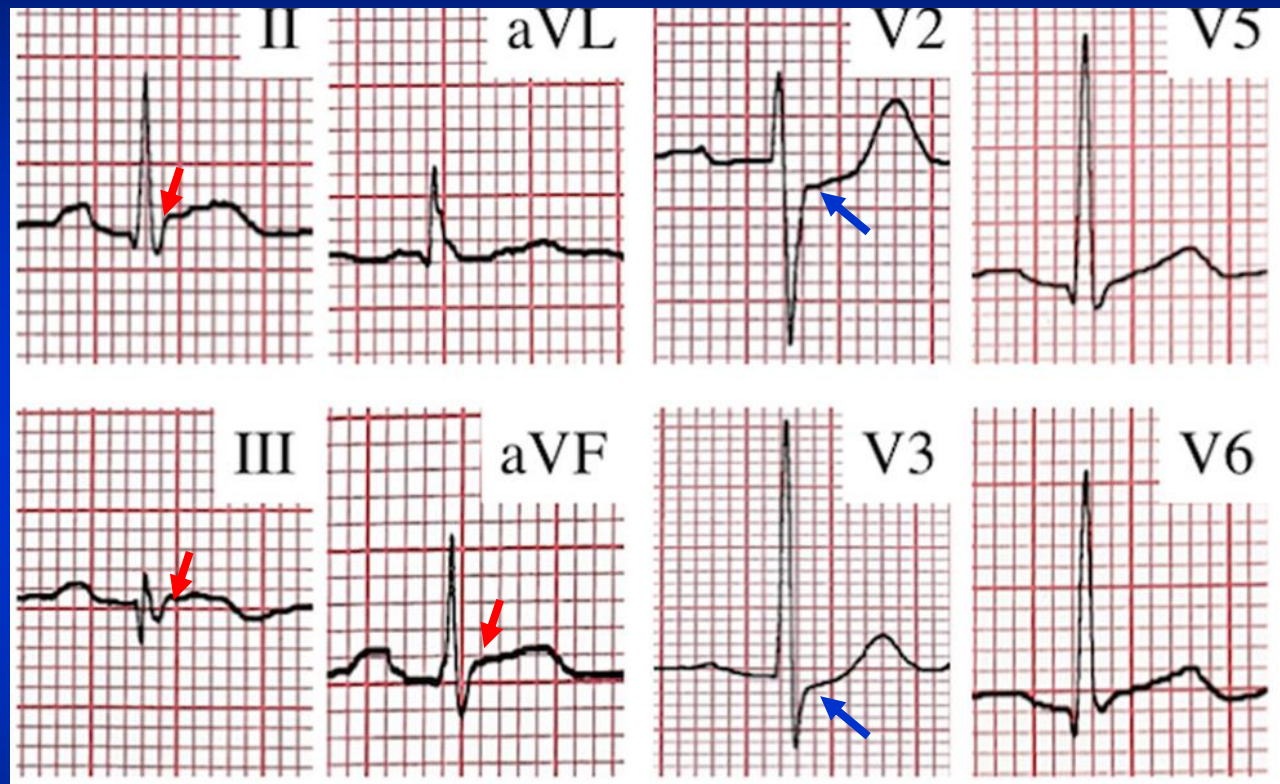


T2 weighted

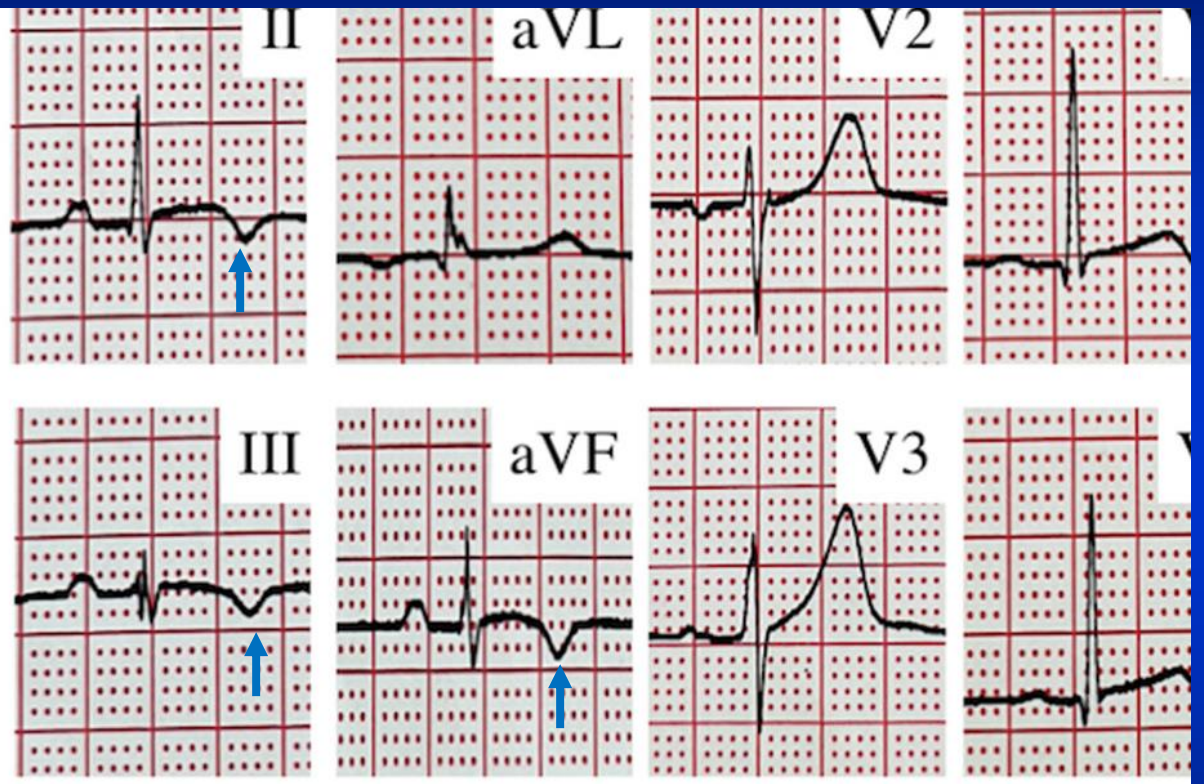
Late gadolinium enhancement

心電圖

住院



出院 (1 週後)

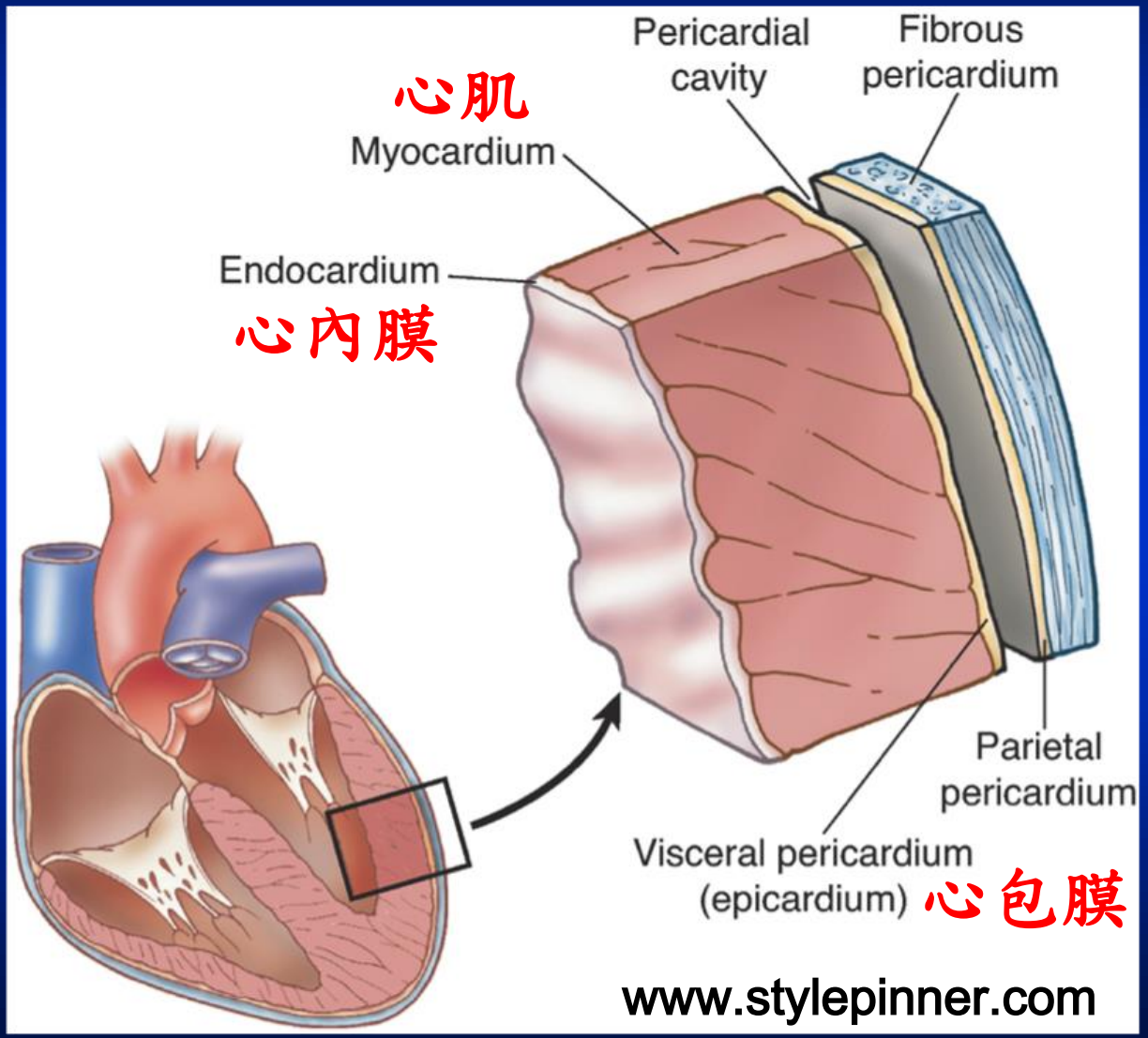


心肌炎12問

1. 什麼是心肌炎?
2. 心肌炎對心臟有什麼影響?
3. 心肌炎有哪些原因?
4. 接種疫苗後心肌炎的發生率?
5. 心肌炎好發於什麼樣的病人?第幾劑?
6. 心肌炎的病理表現?
7. 心肌炎的致病機轉?
8. 心肌炎有什麼早期症狀?
9. 如何診斷心肌炎?
10. 如何治療心肌炎?
11. 心肌炎預後如何?
12. 到底該不該打疫苗?

1

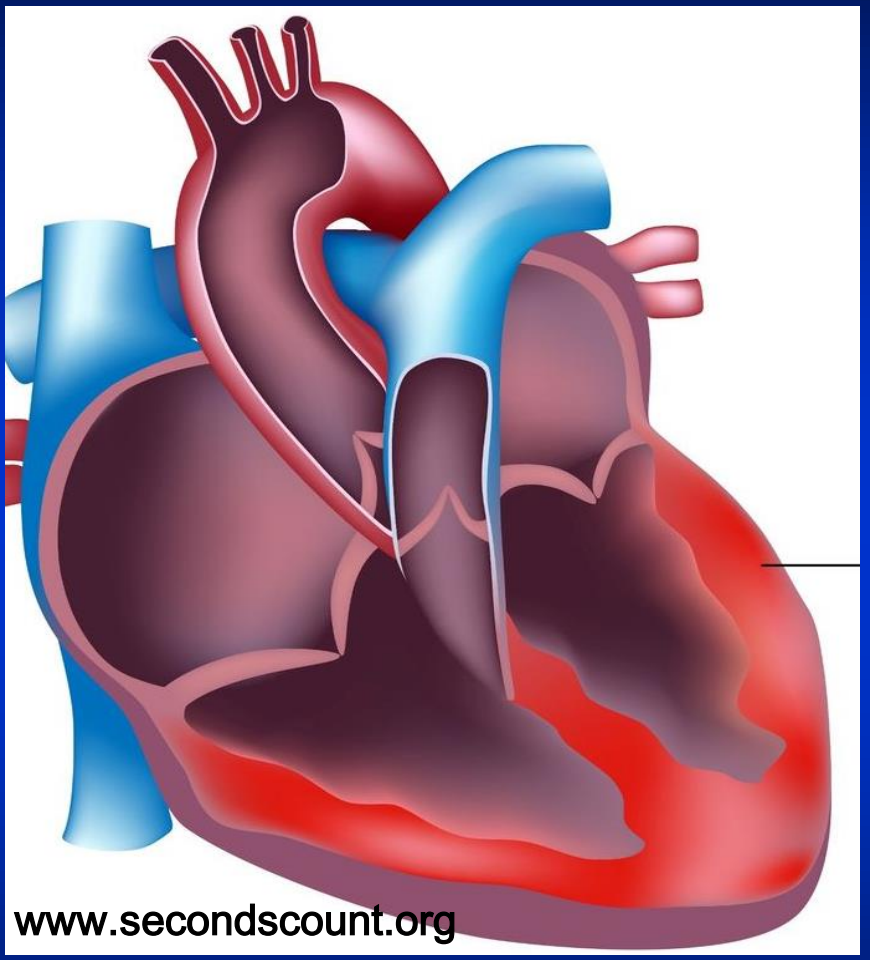
什麼是心肌炎Myocarditis?



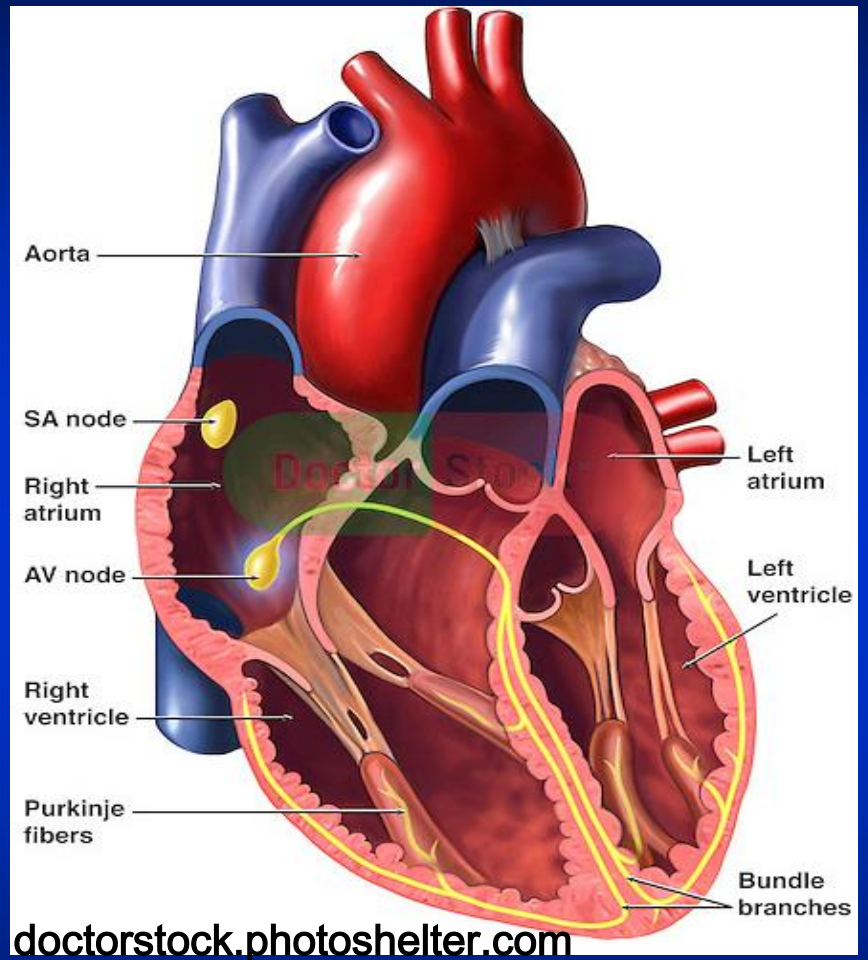
- 心臟主要由肌肉所構成，外表覆以一層心包膜，裡面覆以一層心內膜。
- 心肌炎顧名思義就是心臟的肌肉發炎。
- 有時會合併心包膜炎pericarditis，可以稱作心肌心包膜炎myopericarditis。

2

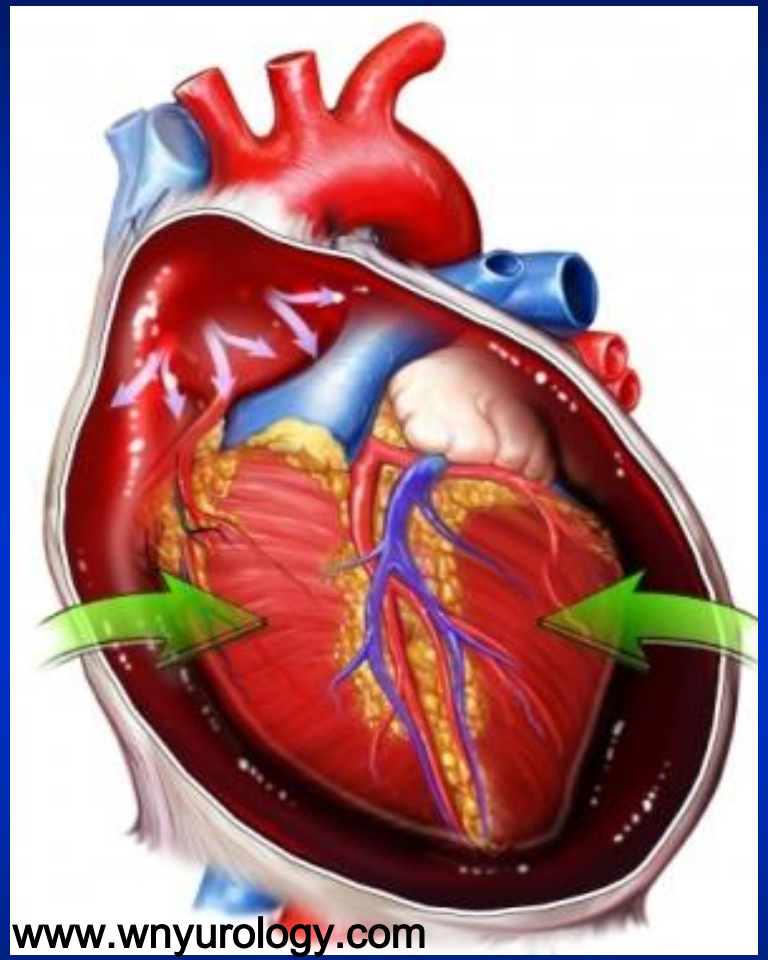
心肌炎對心臟有什麼影響?



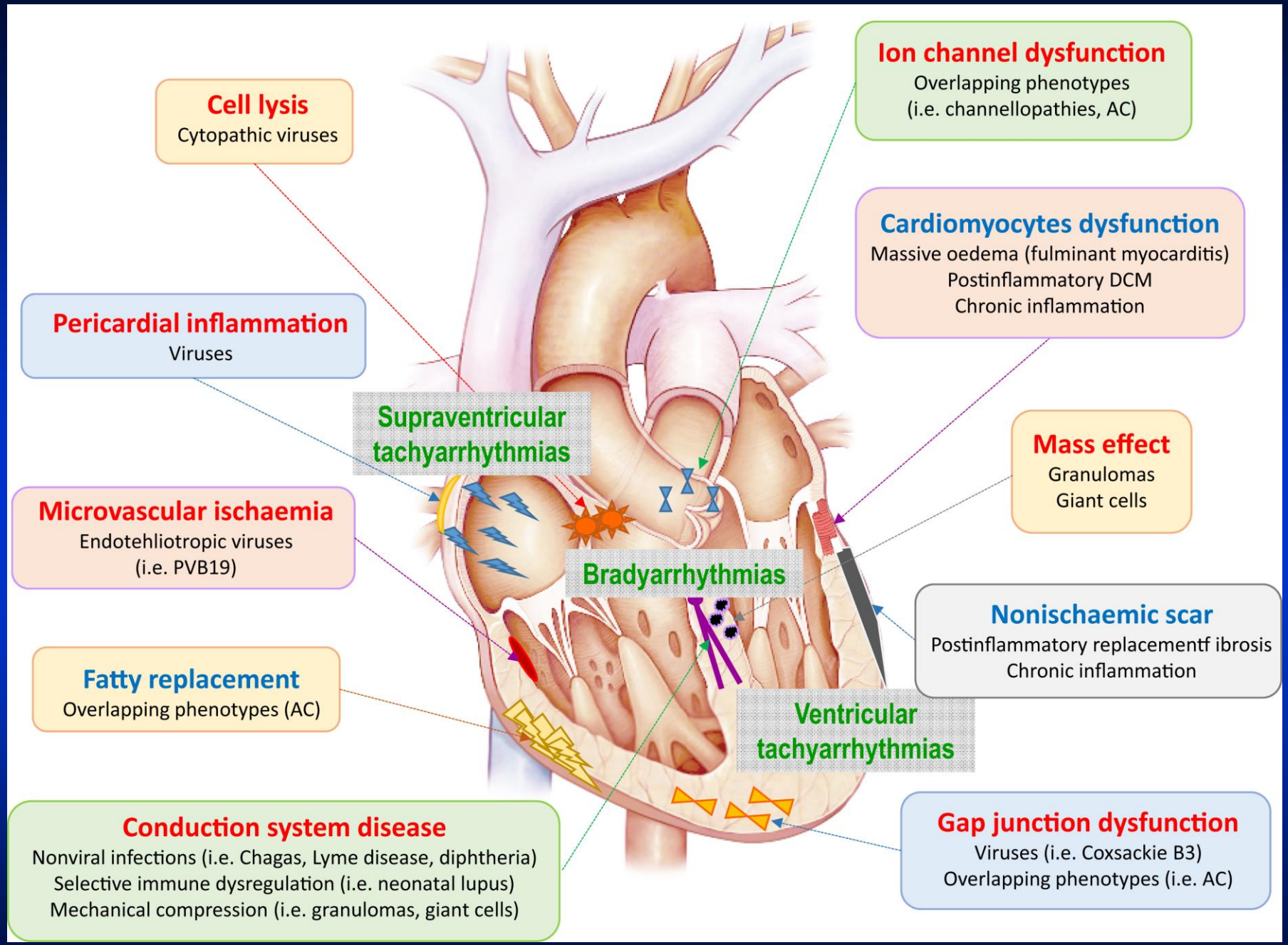
心肌發炎導致心臟收縮不良、心臟擴大



傳導系統發炎導致各式心律不整



心包膜炎導致心包膜腔積液壓迫到心臟



Heart Rhythm. 2019 May;16:793-801

3

心肌炎有哪些原因？

European Society of Cardiology

Table 1 Causes of myocarditis/inflammatory cardiomyopathy

1. Infectious myocarditis	
Bacterial	*Staphylococcus*, *Streptococcus*, *Pneumococcus*, *Meningococcus*, *Gonococcus*, *Salmonella*, *Corynebacterium diphtheriae*, *Haemophilus influenzae*, *Mycobacterium* (tuberculosis), *Mycoplasma pneumoniae*, *Brucella*
Spirochaetal	*Borrelia* (Lyme disease), *Leptospira* (Weil disease)
Fungal	*Aspergillus*, *Actinomyces*, *Blastomyces*, *Candida*, *Coccidioides*, *Cryptococcus*, *Histoplasma*, *Mucormycoses*, *Nocardia*, *Sporothrix*
Protozoal	*Trypanosoma cruzi*, *Toxoplasma gondii*, *Entamoeba*, *Leishmania*
Parasitic	*Trichinella spiralis*, *Echinococcus granulosus*, *Taenia solium*
Rickettsial	*Coxiella burnetii* (Q fever), *R. rickettsii* (Rocky Mountain spotted fever), *R. tsutsugamuschi*
Viral	RNA viruses: Coxsackieviruses A and B, echoviruses, polioviruses, influenza A and B viruses, respiratory syncytial virus, mumps virus, measles virus, rubella virus, hepatitis C virus, dengue virus, yellow fever virus, Chikungunya virus, Junin virus, Lassa fever virus, rabies virus, human immunodeficiency virus-1 DNA viruses: adenoviruses, parvovirus B19, cytomegalovirus, human herpes virus-6, Epstein-Barr virus, varicella-zoster virus, herpes simplex virus, variola virus, vaccinia virus
2. Immune-mediated myocarditis	
Allergens	Tetanus toxoid, vaccines, serum sickness Drugs: penicillin, cefaclor, colchicine, furosemide, isoniazid, lidocaine, tetracycline, sulfonamides, phenytoin, phenylbutazone, methyldopa, thiazide diuretics, amitriptyline
Alloantigens	Heart transplant rejection
Autoantigens	Infection-negative lymphocytic, infection-negative giant cell Associated with autoimmune or immune-oriented disorders: systemic lupus erythematosus, rheumatoid arthritis, Churg-Strauss syndrome, Kawasaki's disease, inflammatory bowel disease, scleroderma, polymyositis, myasthenia gravis, insulin-dependent diabetes mellitus, thyrotoxicosis, sarcoidosis, Wegener's granulomatosis, rheumatic heart disease (rheumatic fever)
3. Toxic myocarditis	
Drugs	Amphetamines, anthracyclines, cocaine, cyclophosphamide, ethanol, fluorouracil, lithium, catecholamines, hemetine, interleukin-2, trastuzumab, clozapine
Heavy metals	Copper, iron, lead (rare, more commonly cause intramyocyte accumulation)
Miscellaneous	Scorpion sting, snake, and spider bites, bee and wasp stings, carbon monoxide, inhalants, phosphorus, arsenic, sodium azide
Hormones	Phaeochromocytoma, vitamins: beri–beri
Physical agents	Radiation, electric shock

4 接種疫苗後心肌炎的發生率?

5 心肌炎好發於什麼樣的病人?第幾劑?

The NEW ENGLAND JOURNAL of MEDICINE

2021 Sep 16;385:1078-1090

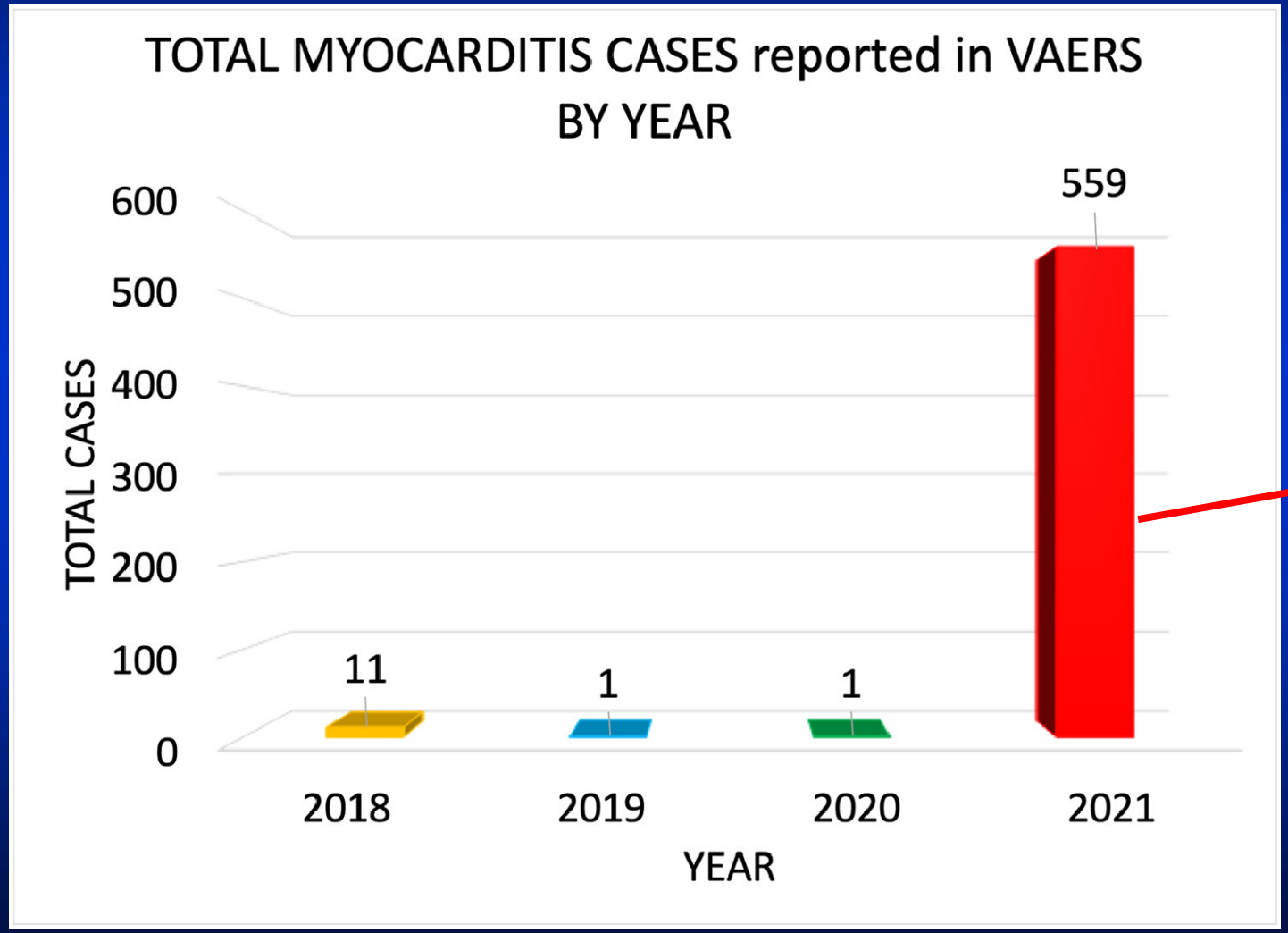
ORIGINAL ARTICLE

Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting

Israel

- Vaccinated and control groups each included a mean of 884,828 persons
- BNT was associated with an excess risk of myocarditis (1-5 per 100,000)
- Risk ratio 3.24 (95% CI 1.55 to 12.44)
- Risk difference 2.7 events per 100,000 persons (95% CI 1.0 to 4.6)

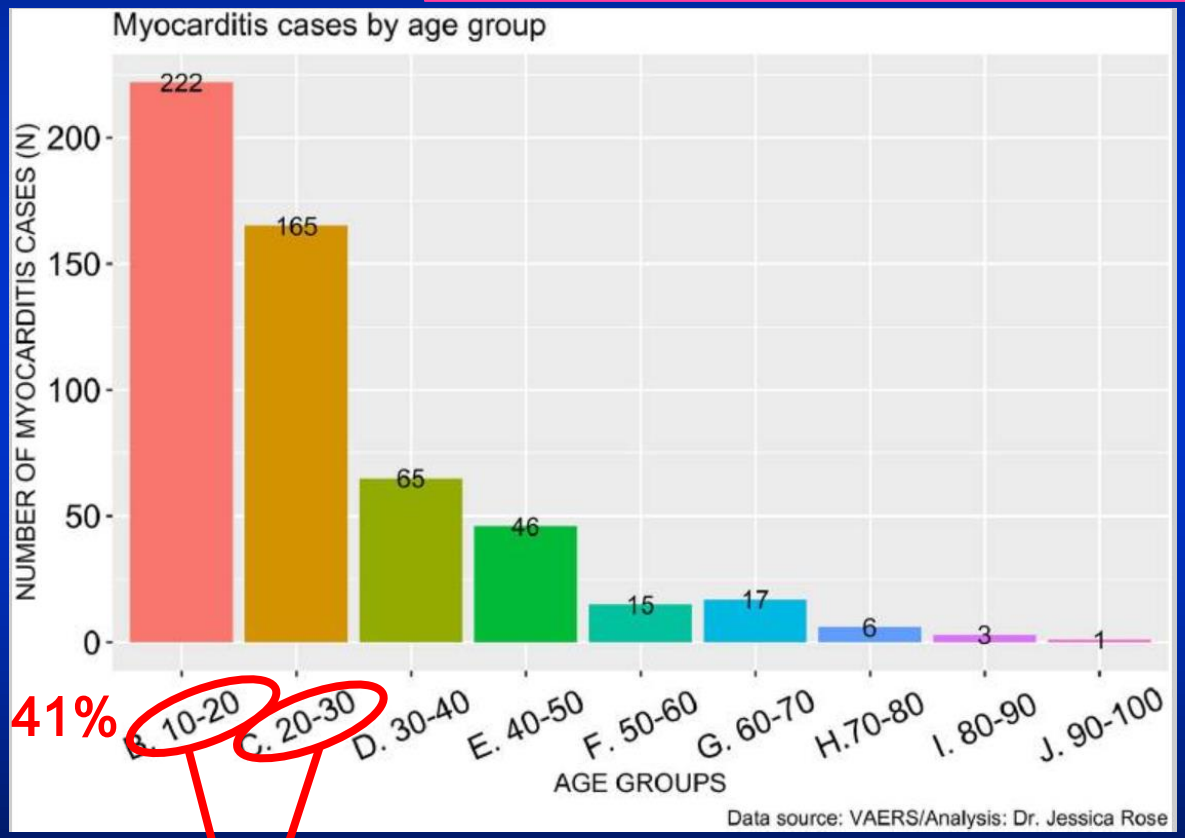
A Report on Myocarditis Adverse Events in the U.S. Vaccine Adverse Events Reporting System (VAERS) in Association with COVID-19 Injectable Biological Products Curr Probl Cardiol. 2021 Sep 30

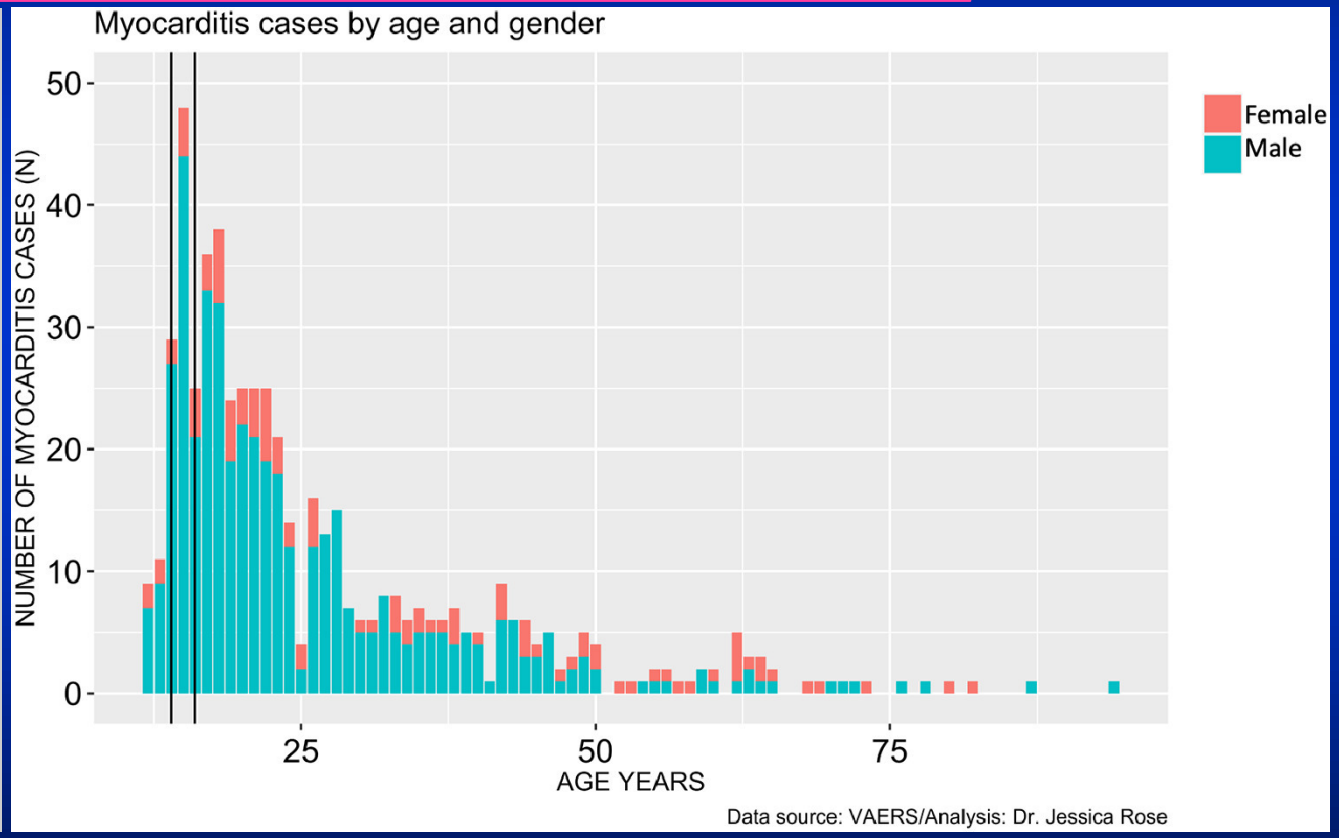


3/1,000,000

A Report on Myocarditis Adverse Events in the U.S. Vaccine Adverse Events Reporting System (VAERS) in Association with COVID-19 Injectable Biological Products Curr Probl Cardiol. 2021 Sep 30

2021年: 559 病例(0.14%通報)、BNT 67%、6例死亡(1.1%)





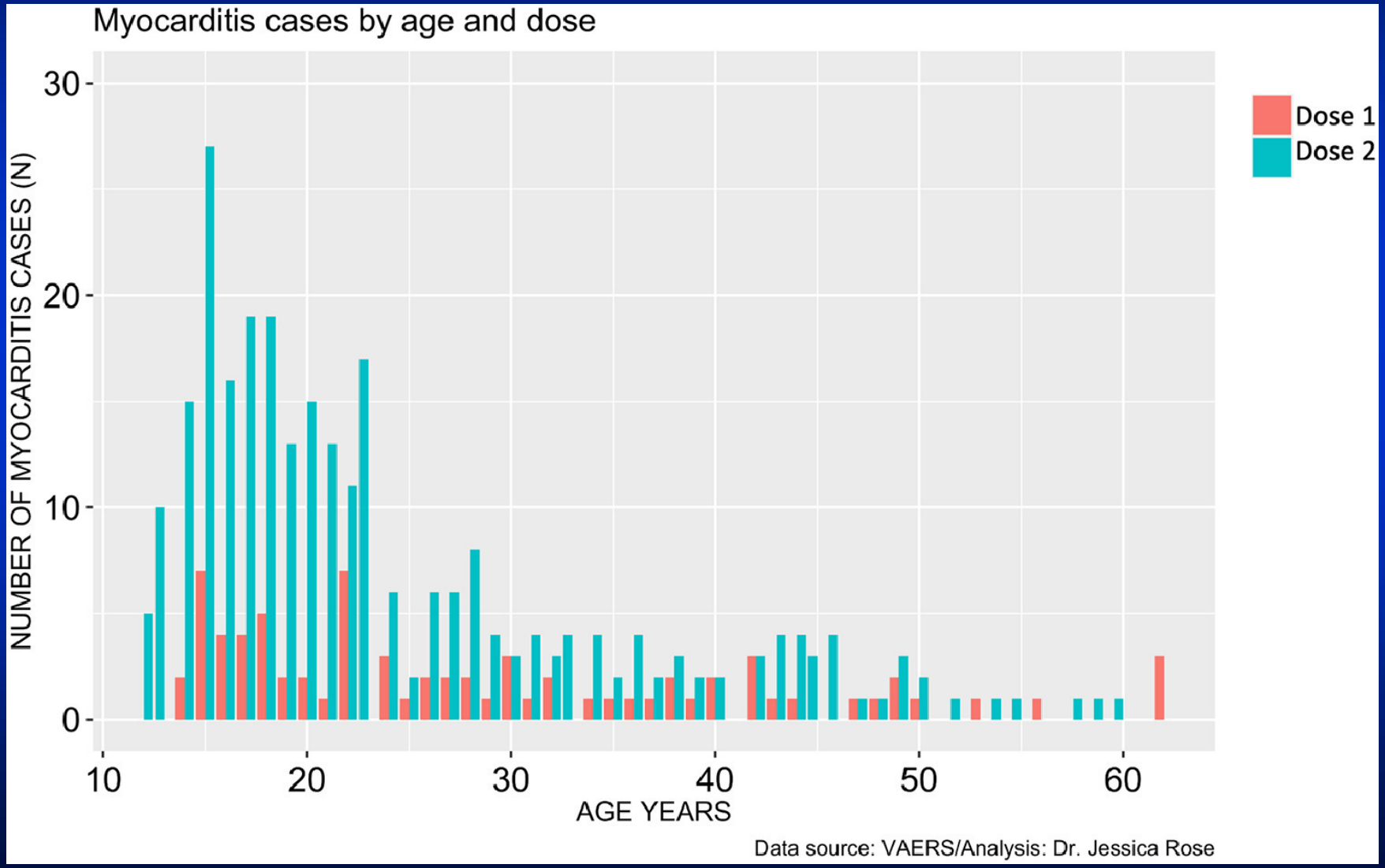
41%

72%

年輕

男性(80%)

A Report on Myocarditis Adverse Events in the U.S. Vaccine Adverse Events Reporting System (VAERS) in Association with COVID-19 Injectable Biological Products Curr Probl Cardiol. 2021 Sep 30



第二劑

JAMA | Original Investigation 2021 Sep 3

Surveillance for Adverse Events After COVID-19 mRNA Vaccination

Table 4. Confirmed Myocarditis/Pericarditis After Receipt of mRNA Vaccines Compared With Vaccinated Comparators Among Individuals Aged 12-39 Years by Dose and Risk Interval, December 14, 2020-June 26, 2021

Risk interval, d[a]	Dose	Events in risk interval (events/million person-years)[b]	Events in 21-d comparison interval[b,c] (events/million person-years)[b,c]	Adjusted rate ratio (95% CI)[d]	2-Sided *P* value	Excess cases in risk interval per million doses (95% CI)[e]
0-21	Both	34 (141.2)	4 (35.0)	3.75 (1.38 to 12.84)	.007	6.2 (2.3 to 7.8)
	1	9 (70.4)	4 (35.0)	3.67 (0.92 to 17.35)	.07	3.1 (-0.4 to 4.0)
	2	24 (221.3)	4 (44.6)	4.07 (1.45 to 14.18)	.005	10.1 (4.1 to 12.4)
0-7	Both	29 (320.8)	4 (35.0)	9.83 (3.35 to 35.77)	<.001	6.3 (4.9 to 6.8)
	1	5 (104.2)	3 (35.0)	7.27 (1.29 to 50.15)	.02	2.0 (0.5 to 2.2)
	2	23 (565.9)	4 (44.6)	10.4 (3.54 to 37.76)	<.001	11.2 (8.9 to 12.1)
8-14	Both	2 (25.7)	4 (35.0)	1.22 (0.14 to 7.74)	.82	0.1 (-3.0 to 0.4)
	1	2 (48.0)	3 (35.0)	3.25 (0.31 to 29.64)	.30	0.6 (-2.0 to 0.9)
	2	0	4 (44.6)	0 (0 to 3.22)	.28	-0.9 (-0.9 to 0)
15-21	Both	3 (41.3)	4 (35.0)	1.55 (0.28 to 7.78)	.58	0.3 (-2.0 to 0.7)
	1	2 (52.3)	4 (35.0)	2.58 (0.27 to 18.62)	.37	0.6 (-2.7 to 0.9)
	2	1 (29.1)	4 (44.6)	0.67 (0.03 to 5.64)	.79	-0.3 (-21.2 to 0.5)

71%

85%

Circulation

PRIMER

Myocarditis With COVID-19 mRNA Vaccines

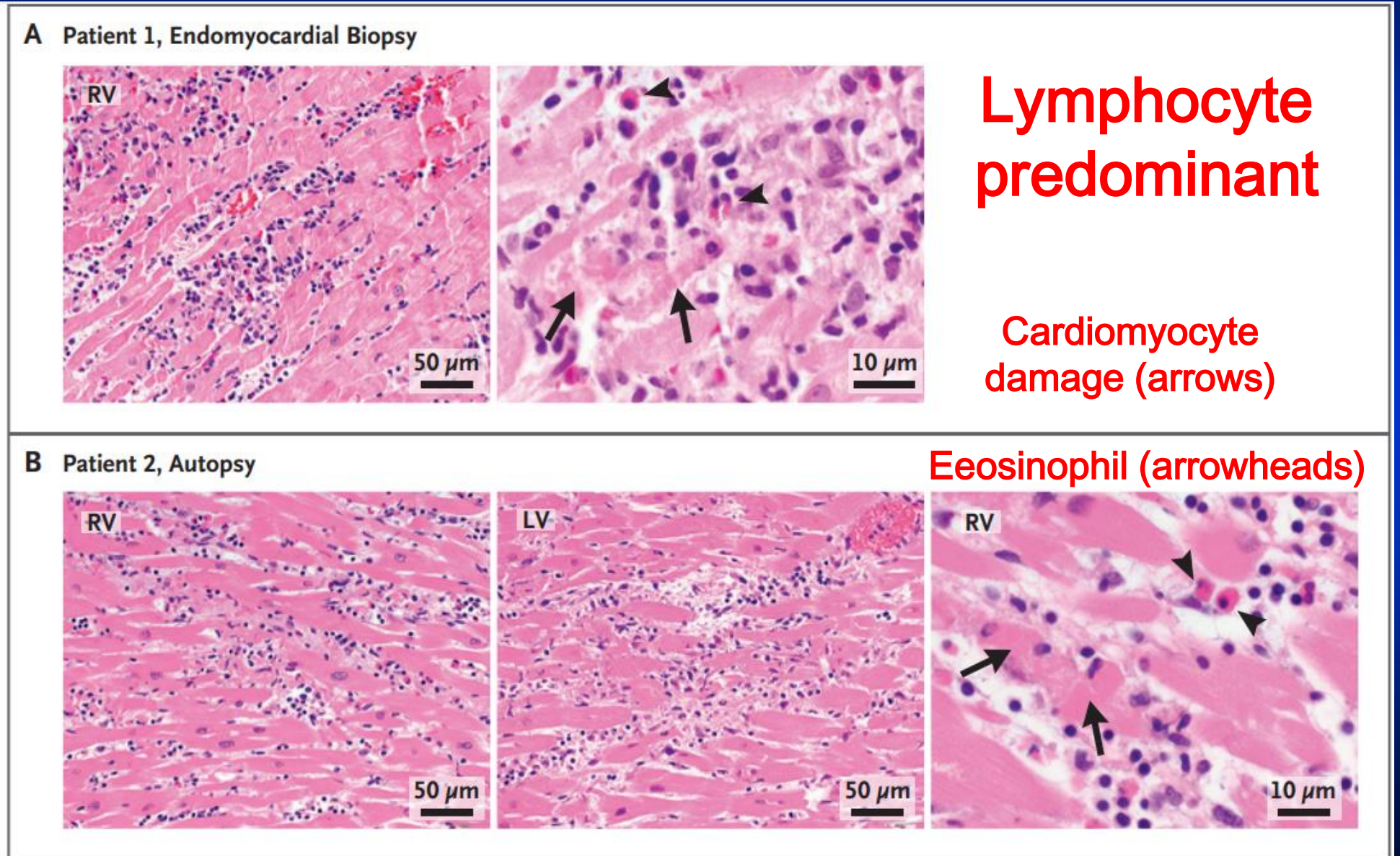
2021 Aug 10; 144(6): 471–484.

Age groups	Female rates per million doses			Male rates per million doses		
	All doses	Dose 1	Dose 2	All doses	Dose 1	Dose 2
12–17 y	4.2	1.1	9.1	32.4	9.8	66.7
18–24 y	3.6	1.5	5.5	30.7	8.7	56.3
25–29 y	2.0	0.8	2.6	12.2	4.5	20.4
30–39 y	1.8	1.4	1.8	6.9	2.0	10.0
40–49 y	2.0	0.9	2.8	3.5	1.0	5.1
50–64 y	1.6	1.0	1.8	1.9	1.0	2.3
65+ y	1.1	0.6	1.2	1.2	0.7	1.4

6

心肌炎的病理表現?

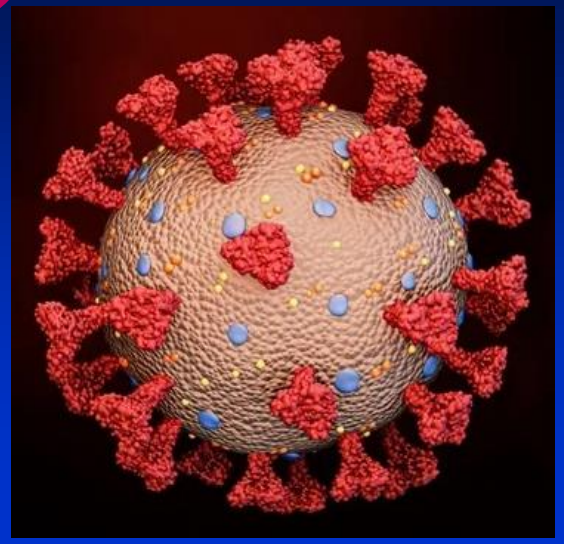
N Engl J Med. 2021 Aug 18



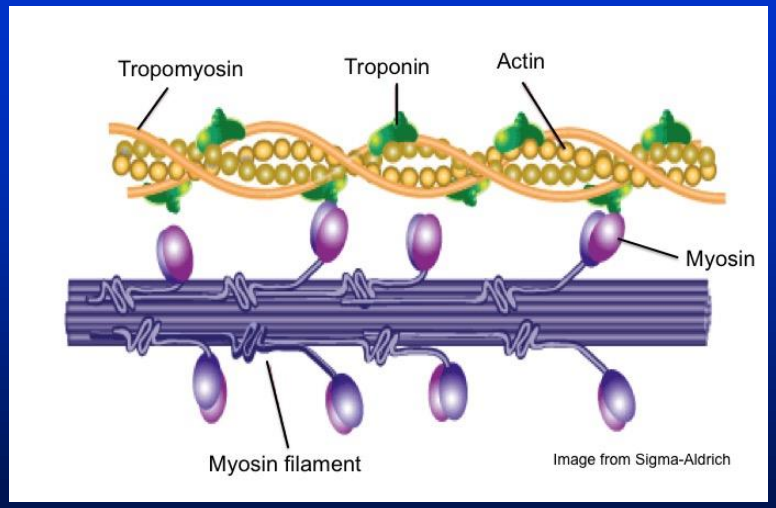
7

心肌炎的致病機轉？

Circulation 2021 Aug 10; 144: 471–484



MattLphotography/Shutterstock.com



www.crossfitinvictus.com

- The mechanism for vaccine induced myocarditis remains unclear.
- Molecular mimicry between the spike protein and self-antigens. Antibodies against spike protein have been experimentally shown to cross-react with structurally similar human peptide protein sequences, including α-myosin.
- Vaccine may trigger preexisting dysregulated pathways in certain individuals with predisposition, resulting in a polyclonal B-cell expansion, immune complex formation, and inflammation.

8

心肌炎有什麼早期症狀?

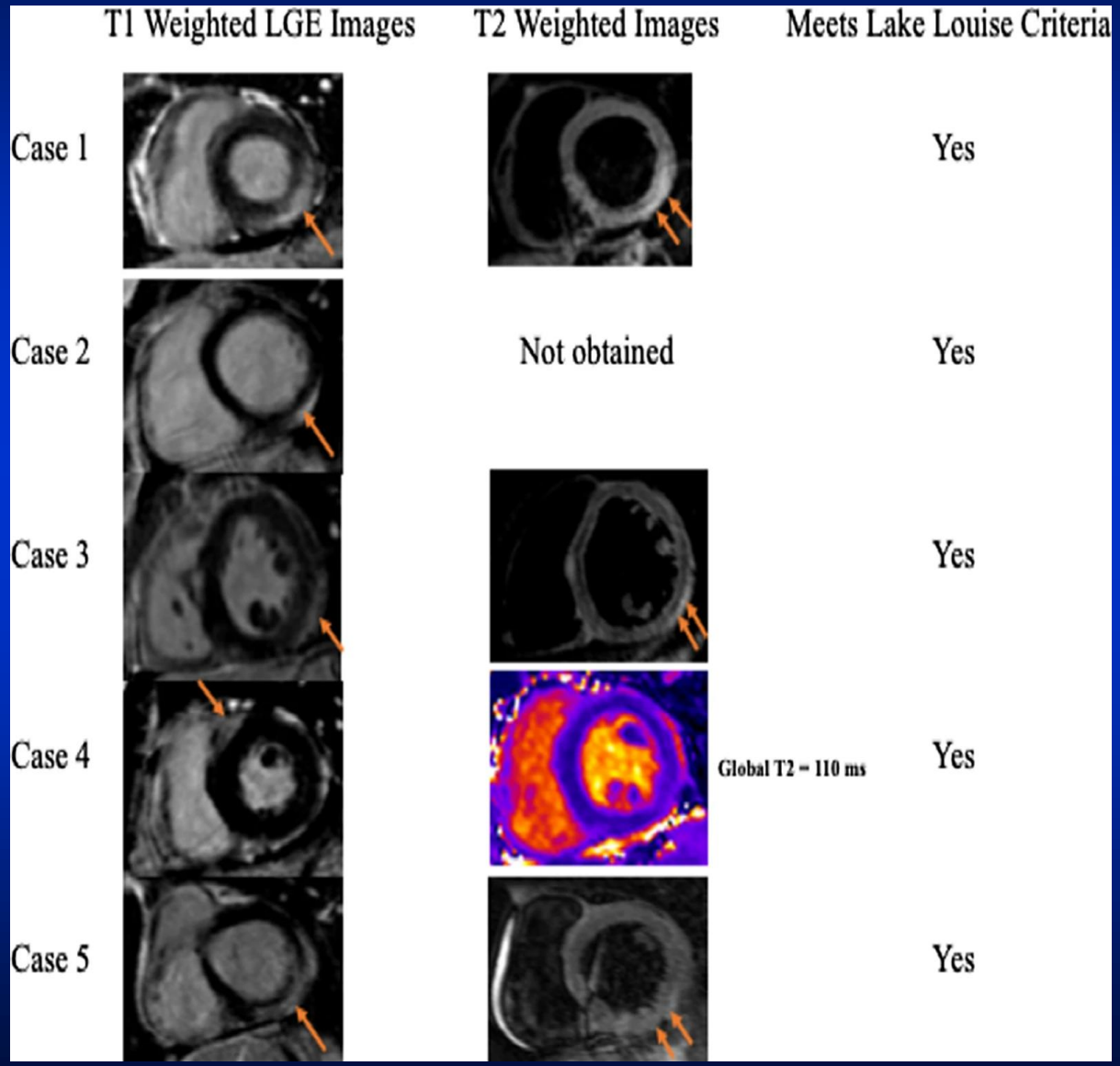
1. 胸痛、胸口壓迫感、胸悶
2. 心悸、心跳過快或過慢、不規則
3. 呼吸急促或困難
4. 運動耐受不良、體力變差
5. 暈厥、昏厥

9

如何診斷心肌炎？

- 病史
- 理學檢查
- 抽血
  - 心肌酵素 Troponin, CKMB
  - 發炎指數 CRP, ESR
  - 心衰指數 BNP/NT-pro-BNP
- 心電圖
- 胸部X光
- 心臟超音波
- 心臟核磁共振
- 心導管
- 心肌切片

心臓核磁共振



- Myocardial edema in the lateral wall of the left ventricular myocardium
  - LGE (Late gadolinium enhancement) on T1-weighted images
  - Hyperintense signal on T2-weighted fat suppressed images
  - Elevated relaxation time (normal range < 60 ms)
- Reduced global LV longitudinal strain

J Cardiovasc Magn Reson. 2021 Sep 9;23:101

CDC Working Case Definitions

Acute Myocarditis

Probable Case

- Presence of ≥ 1 new or worsening of the following clinical symptoms
  - chest pain/ pressure/ discomfort
  - dyspnea/shortness of breath
  - palpitations
  - syncope
- AND ≥ 1 new finding of
  - elevated troponin above upper limit of normal
  - abnormal ECG or rhythm monitoring findings consistent with myocarditis*
  - abnormal cardiac function or wall motion abnormalities on echocardiogram
  - cardiac MRI findings consistent with myocarditis†
- AND no other identifiable cause of the symptoms and findings

Confirmed Case

- Presence of ≥ 1 new or worsening of the following clinical symptoms
  - chest pain/ pressure/ discomfort
  - dyspnea/shortness of breath
  - palpitations
  - syncope
- AND
  - histopathologic confirmation of myocarditis ‡
  - OR
  - elevated troponin above upper limit of normal AND cardiac MRI findings consistent with myocarditis†
- AND no other identifiable cause of the symptoms and findings

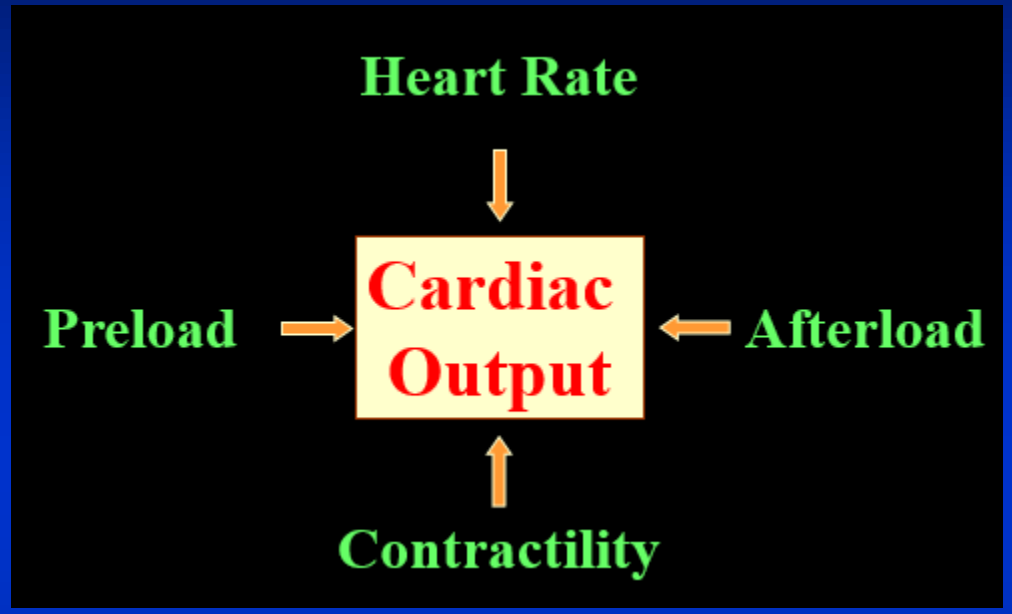
Acute Pericarditis

Probable Case

- Presence of ≥ 2 new or worsening of the following clinical symptoms
  - acute chest pain (typically described as pain made worse by lying down, deep inspiration, cough, and relieved by sitting up or leaning forward, although other types of chest pain may occur) §
  - pericarditis rub on exam
  - new ST-elevation or PR-depression on ECG
  - new or worsening pericardial effusion on echocardiogram or MRI
- Autopsy cases may be classified as pericarditis on basis of meeting histopathologic criteria of the pericardium

如何治療心肌炎?

- Heart failure therapy
- Arrhythmia therapy
  - Tachyarrhythmia
  - Bradyarrhythmia
- Anti-inflammation
  - IVIG
- Mechanical circulatory support
  - LVAD、ECMO



11

心肌炎預後如何?

EDITORIAL

JAMA Intern Med. 2021 Oct 4

COVID-19 Messenger RNA Vaccination and Myocarditis—A Rare and Mostly Mild Adverse Effect

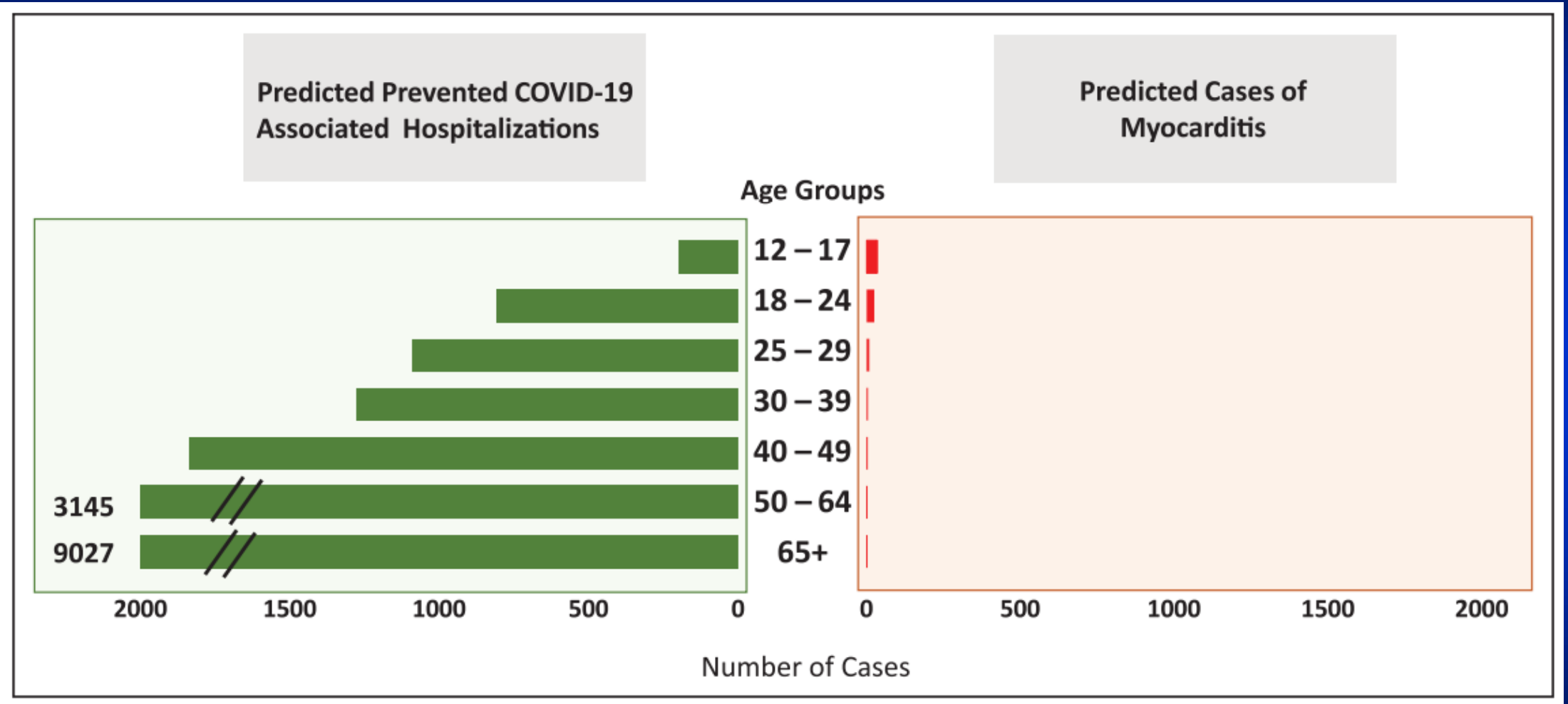
Vinay Guduguntla, MD; Mitchell H. Katz, MD

Several recent case series have described acute myocarditis after COVID-19 messenger RNA (mRNA) vaccination.[1,2] While the cardiac complications of vaccines are important, discussion has been limited by small sample sizes that lack gender and racial and ethnic diversity. In this issue of *JAMA Internal Medicine*, Simone et al[3] examine the incidence and outcomes of acute myocarditis following COVID-19 mRNA vaccination in a large community health system. During the 6 months of follow-up, there were 15 cases of myocarditis among the 2 392 924 Kaiser Permanente Southern California members who received at least 1 dose of the Pfizer and Moderna vaccines (1 case per 172 414 fully vaccinated individuals). This represents a relative ratio of 2.7 compared with unvaccinated individuals. The study population was 54.0% women and 31.2% White, 6.7% Black, 37.8% Hispanic, and 14.3% Asian individuals. Interestingly, the affected patients were all men younger than 40 years with no prior cardiac history, and they were discharged within a week of conservative management.[3] These results parallel prior studies that showed incidence of post–COVID-19 mRNA vaccination myocarditis primarily in young men who have recently received their second vaccine dose.[1]

+ Related article

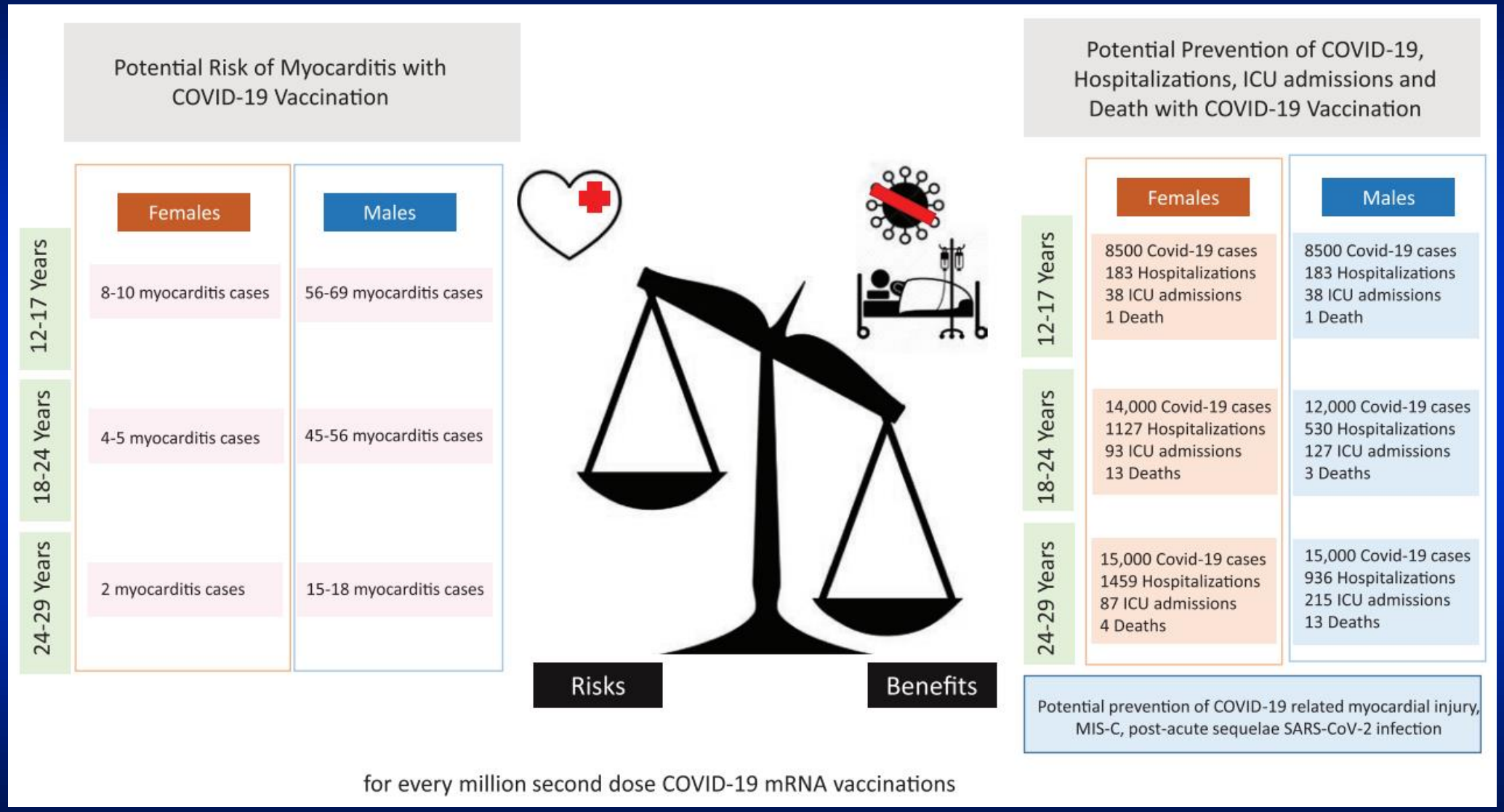
Overall, vaccination-related myocarditis was a rare and mostly mild adverse event. Data from the Vaccine Adverse Event Reporting System indicate that it is not unique to just the COVID-19 mRNA vaccine.[4] Moreover, this risk is small when weighed with the morbidity and mortality of COVID-19 infection, in which up to 28% of hospitalized patients showed signs of myocardial injury.[5] Randomized clinical trials show that COVID-19 mRNA vaccines represent a safe and effective method of preventing infection; the identification of rare myocarditis does not change clinical decision-making. However, it would be worthwhile to identify the mechanism of cardiac injury from vaccines. In addition, we anticipate seeing more cases of myocarditis, as vaccination was recently approved for teenage males aged 12 to 16 years.

到底該不該打疫苗?



Circulation 2021 Aug 10; 144: 471–484

到底該不該打疫苗？



Circulation 2021 Aug 10; 144: 471–484

結論(1)

- 接種疫苗後極少數人(小於萬分之1)發生心肌炎
- 心肌炎好發於年輕、男性、第二劑
- 症狀大多發生於疫苗施打後一週內
  1. 胸痛、胸口壓迫感、胸悶
  2. 心悸、心跳過快或過慢、不規則
  3. 呼吸急促、困難
  4. 運動耐受不良、體力變差
  5. 暈厥、昏厥
- 診斷: 心電圖、心肌酵素、心臟超音波、核磁共振等
- 治療: 大部份是輕症、短時間可恢復

結論(2)

- 考量利弊得失，絕大多數人還是建議應該施打疫苗
- 以下狀況需更仔細評估
  - 最近六個月內曾發生心肌炎、心包膜炎、心內膜炎
  - 急性風濕熱或風濕性心臟病
  - 30歲以下年輕人合併擴大型心肌病變
  - 複雜或嚴重型先天性心臟病(如單一心室等)
  - 急性心臟衰竭病人
  - 心臟移植病患

願上帝祝福大家！