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Covid-19 Pandemic and Cardiac Arrhythmia

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Introduction

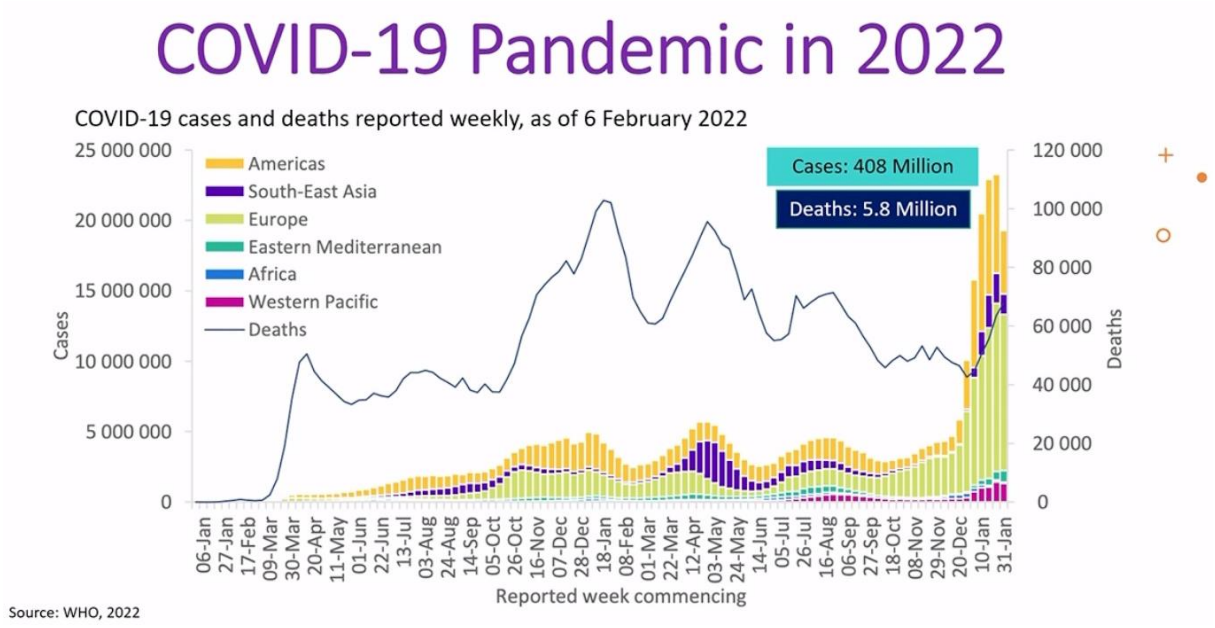
The Covid -19 pandemic, has affected the whole world.

The clinic manifestations are primarily respiratory with an acute respiratory distress syndrome (ARDS).

But this virus can affect different organs including the heart with rhythmic complications.

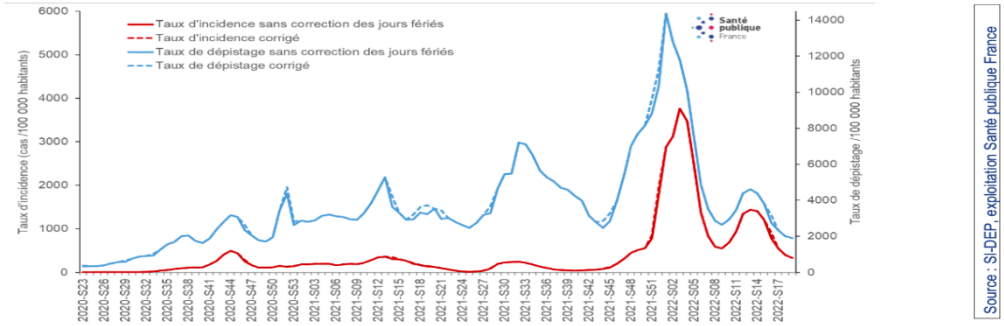
Epidemiology: (54)

This pandemic has affected more than 500 million people worldwide. And was responsible for the deaths of more than 6 million.



Incidence and screening according to age :(29,40,41,44,54)

Évolution des taux d'incidence et de dépistage par semaine, avec ou sans correction pour l'effet des jours fériés depuis la semaine 23-2020, France (données au 18 mai 2022)



Incidence et dépistage par classe d'âge

En S19, le taux d'incidence a diminué dans l'ensemble des classes d'âge, de -6% chez les 10-19 ans à -31% chez les 90 ans et plus. Les 30-39 ans avaient le taux le plus élevé (400, -17%), suivis par les 70-79 ans (387, -23%). Les taux les plus bas (inférieurs à 300) étaient observés chez les moins de 20 ans et les 80-89 ans. Le taux de dépistage a diminué chez les 20 ans et plus, il était stable chez les 10-19 ans (1 217, -1%) et a augmenté chez les 0-9 ans (1 335, +11%). Les taux les plus élevés étaient observés chez les 70-79 ans (2 436, -6%) et les 90 ans et plus (2 432, -16%). Le taux de positivité a diminué dans toutes les tranches d'âge, de -1,0 point chez les 10-19 ans à -3,8 points chez les 0-9 ans. Il était inférieur à 20% dans toutes les classes d'âge sauf chez les 40-49 ans (20,1%, -2,5 points). Il était le plus bas chez les 90 ans et plus (12,9%, -2,8 points). Chez les enfants d'âge scolaire, le taux d'incidence a diminué dans toutes les tranches d'âge excepté chez les 6-14 ans où il est resté stable. Le taux de dépistage a augmenté chez les 3-14 ans et a diminué chez les 0-2 ans et les 15-17 ans. Le taux de positivité était en baisse dans toutes les classes d'âge. Le taux d'incidence était le plus haut chez les 6-10 ans (287, -1%) avec un taux de dépistage de 1 541 (+19%) et un taux de positivité de 18,6% (-3,9 points).

Incidence of cardiac arrhythmia (2,3,8,32)

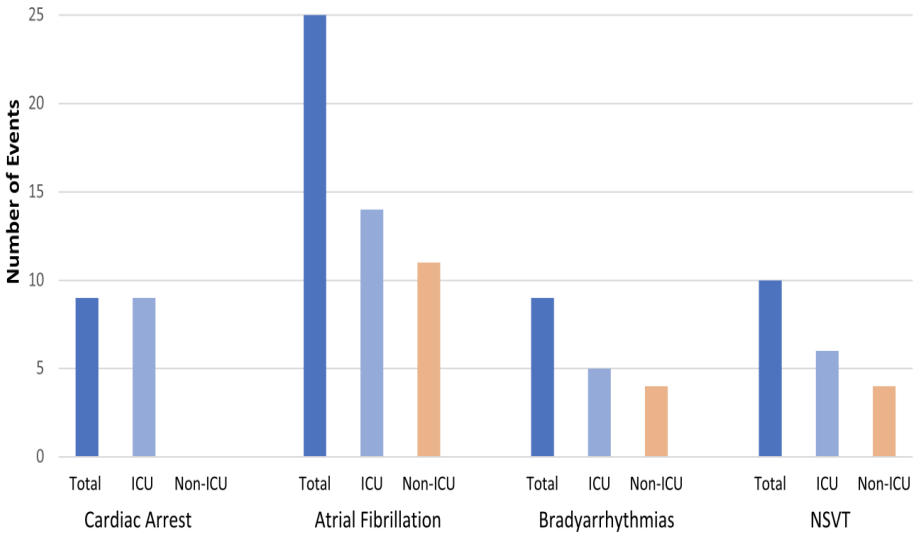
• The incidence of rhythm and conduction disorders during Covid-19 infection is estimated at 17% (11% if it's the Omicron virus) of hospitalized patients. It is 44% of patients hospitalized in intensive care unit (ICU) .

• Atrial fibrillation represents the most frequent arrhythmia with more than 50% depending on the series (40 to 70%). After these are ventricular arrhythmia with an average frequency of 15%, and in the third conductive disorders.

Number of events according intensive care unit (ICU) hospitalization or non (ICU):

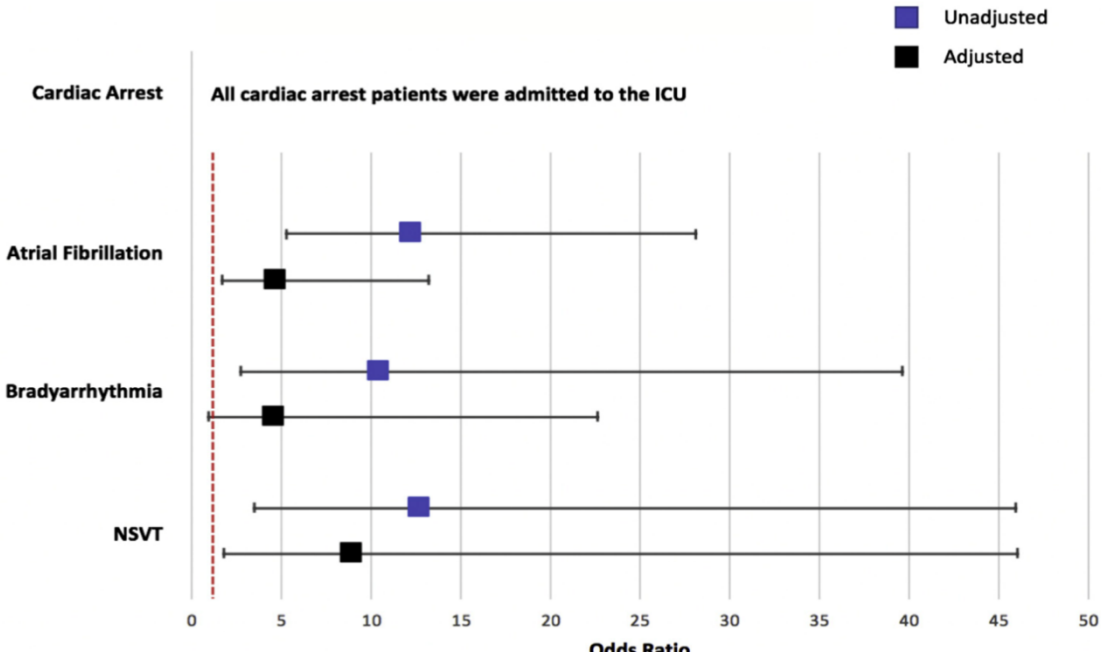
(2,3,,15,18,24,25,32)

Arrhythmias are very frequent hospitalization in intensive care, testifying to the seriousness of their existence during this condition. Here is a study by



Association of intensive care unit (ICU) status and cardiac arrhythmias:(3,15,24).

In the intensive care unit, the most serious arrhythmias are the most frequent, such as ventricular arrhythmias.



Association of intensive care unit (ICU) status and cardiac arrhythmias. The odds ratios (and 95% confidence intervals) of ICU admission and specified cardiac arrhythmias are depicted. The dashed vertical red line represents an odds ratio 5 1. Unadjusted models have a blue marker. Multivariable models (black marker) were adjusted for age, sex, race, body mass index, heart failure, coronary heart disease, diabetes, hypertension, chronic kidney disease, and hydroxychloroquine treatment. NSVT 5 non sustained ventricular tachycardia.

Arrhythmias reported in Covid-19 hospitalization:(3,6,24,28,45,53).

Authors Country	Study Type	Numbers of patients population	Numbers of patients with arrhythmia	Arrhythmia type	Prognosis	
Mehra and All International	Observational	8910	304 (3,4%)	Not specifed	6,8% of patients die and 3,2% having survived	
Goyal and All USA	Observational	393	29 (7,5%)	Atrial arrhythmia 17,7% Invasive ventilation and 1,9% others		
Wang and All China	Observational	138	23 (16,7%)		44% In ICU 6,9% Others	
Guo and All	Case study	187	11 (5,9%)	VT/VF	11,5% Troponine (+) and 5,2 Troponine (-)	

Prognosis of cardiac arrhythmia in patient with covid-19:

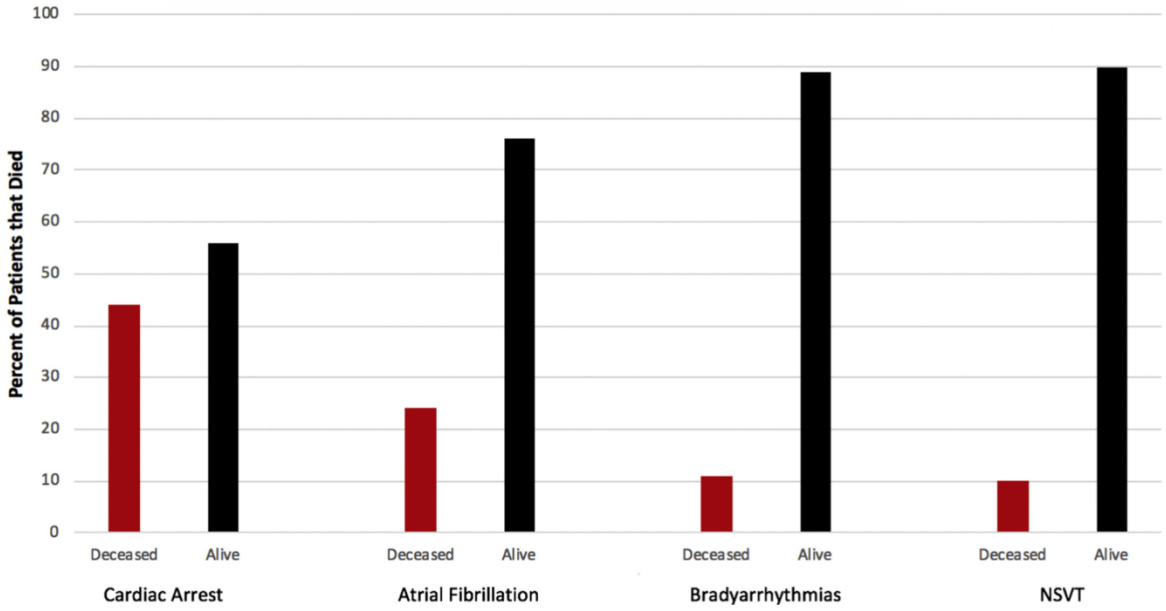
The prognosis is poor if an arrhythmia is associated with covid-19. these arrhythmias are a marker of the severity of the viral attack linked to several mechanisms.

- According to the series, mortality can reach 80%, especially in ICU patients.
- Direct attack by the virus (myocarditis or pericarditis).

Indirect harm :

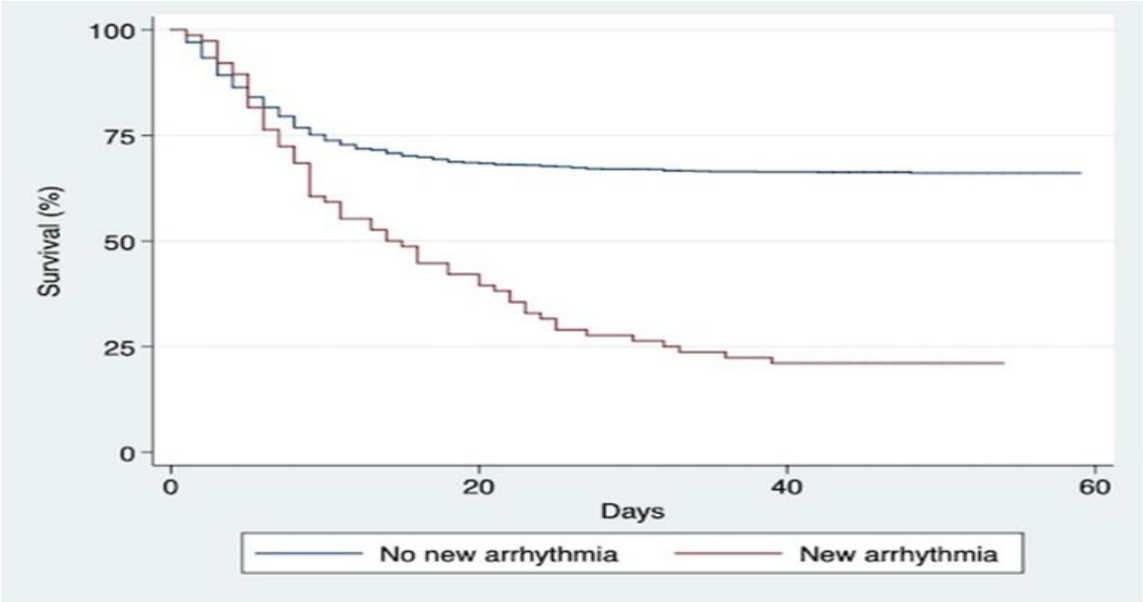
- Severe hypoxemia (ARDS).
- Severe inflammatory reaction(cytokine storm).
- Hydroelectrtolytic disorder and or medications.

Death rate by arrhythmia :(3,15,24)



Arrhythmia Survival rate is new or not:(31).

Patients who develop a heart rhythm disorder for the first time during Covid-19 have a worse prognosis with a mortality rate of around 75% in several series like this.



Risk of death according to age in Covid-19:(21,40,41,44).

The mortality rate is higher in the age group between 50 and 70 years. It is between 16% (16 patients out of 102) in the age group 50 to 60 years and 26% (23 patients out of 89) in the age group between 60 and 70 years.

Results of the evaluation of patients with COVID-19 symptoms in various age ranges from 24 February 2020 to 24 March 2020 in the three studied hospitals.

Age range (years old)	Suspected cases (No.)	Positive cases (No.)	Recovered cases (No.)	Death (No.)
0–9	13	2	1	0
10–19	34	16	9	0
20–29	96	69	32	3
30–39	124	95	62	5
40–49	153	118	54	13
50–59	161	102	57	16
60–69	126	89	41	23
70–79	56	42	22	13
> 80	27	24	10	7

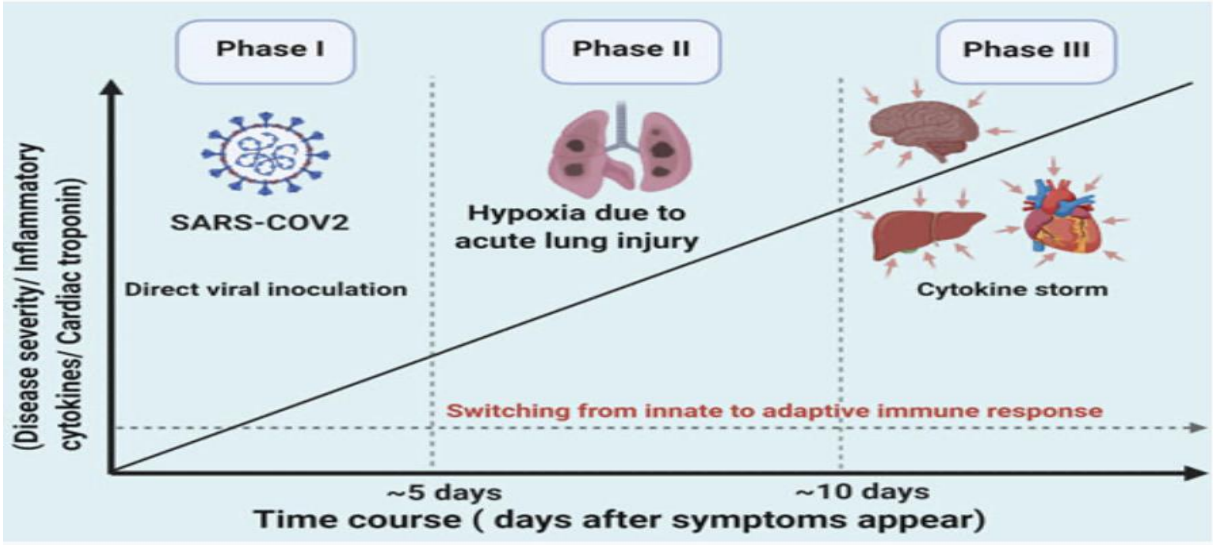
Evolution of the disease after infection with the virus and Cardiac arrhythmia mecanisme. (15,18)

Once infected by the virus, there are 3 evolutionary phases in the mechanism of the appearance of complications, in particular cardiac arrhythmias.

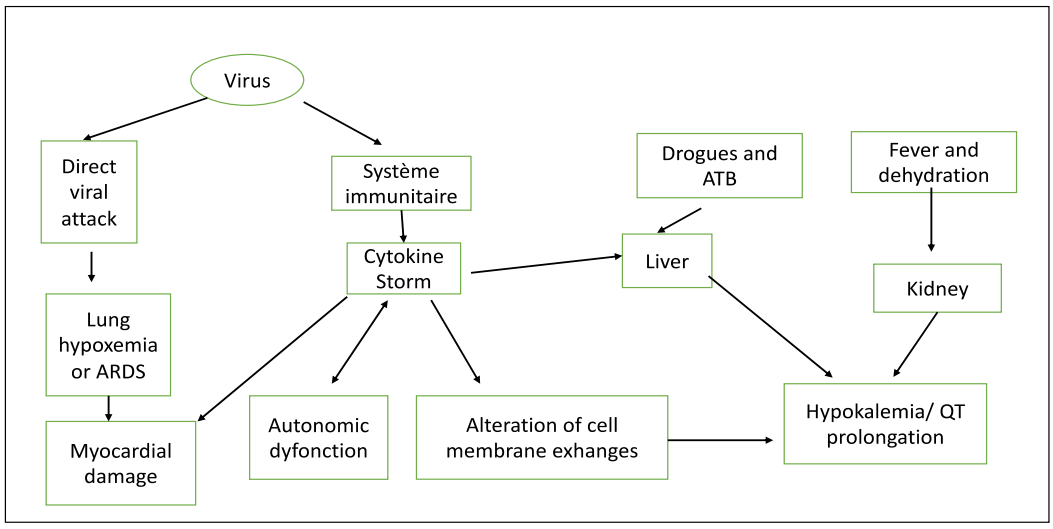
1. phase of contact with the virus of 5 days.

2. Phase of onset of respiratory disorders with 5-day hypoxemia.

3. Inflammatory phase with cytokine storm with multi-organ damage lasting 5 days.



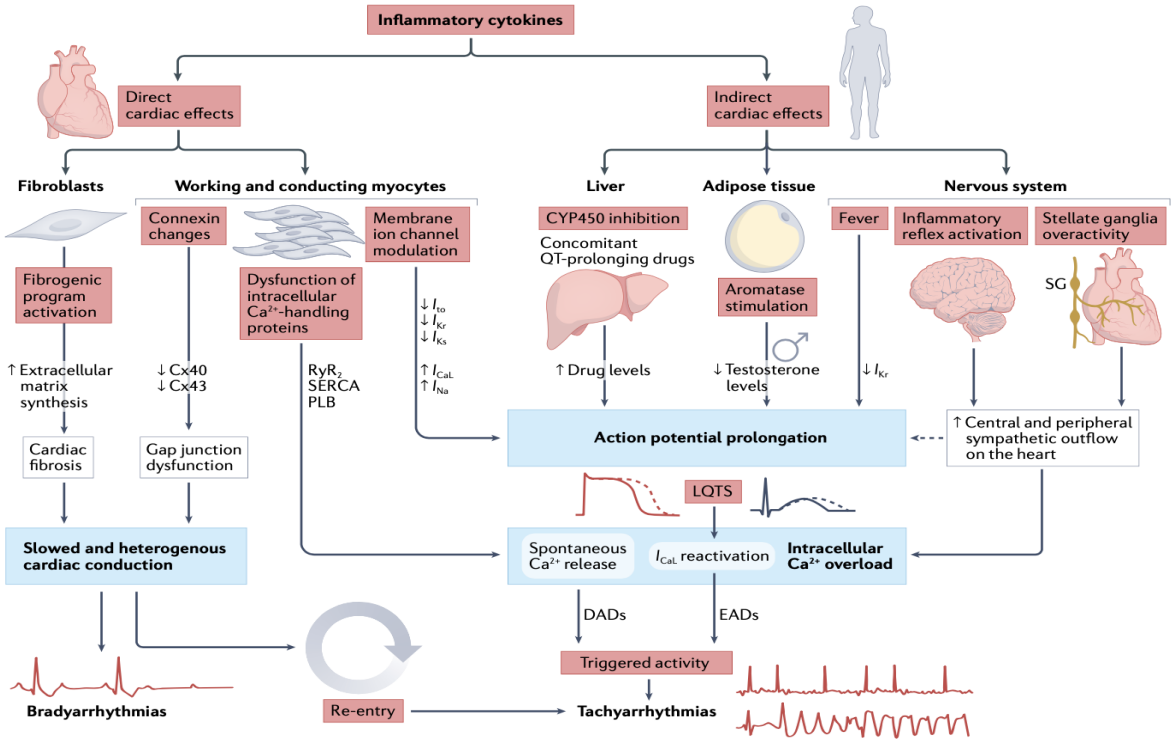
Cardiac arrhythmic mecanisme



Inflammatory mechanism (cytokine storm):(9,10,12,13,14,18,21,26,32,39).

There are two mechanisms

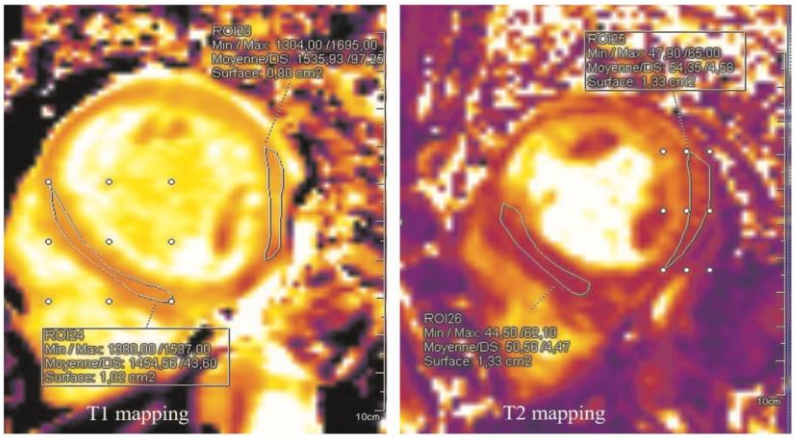
- A direct mechanism or direct attack by the pulmonary and myocardial virus (fibroblast and myocytes).
- An indirect inflammatory mechanism through cytokines. This inflammation can trigger a cytokine storm with hepatic and central nervous system damage as described in this table.



MRI imaging: (34)

Example MRI image

65-year-old woman with confirmed COVID-19 infection and acute myocarditis confirmed by cardiac MRI. T1 mapping sequencespre-injection and T) mannina in favor of important oedema
increase in T1 to T2
T1 : 1154 ms (normal value on 2T < 1256 ms) and
T2 at 50 ms (normal value on 3T < 39 ms).



We see a hypersignal on the sequence T1 and T2 testifying to the edema induced by the inflammatory reaction due to the release of cytokine.

Electrocardiographic aspects:(15,16,36,37,46,47)

Sinus dysfunction (bradycardia).

Sinus tachycardia.

Supra ventricular tachycardia.

Atrial fibrillation or atrial flutter.

Ventricular premature complexes and nonsustained VT.

Conduction disturbances (AVB/BBB).

Polymorphic ventricular tachycardia (torsade de pointe).

Unstable ventricular tachycardia or ventricular fibrillation.

ECG manifestations according to the hospitalization unit: (15,16)

12 lead ECG and rhythm strip in all hospitalized COVID-19 patients
ECG monitoring of COVID-19 patients in case of: – Nonsustained VTs – New-onset atrial fibrillation and flutter – New AVB/BBB – New QTc prolongation >0.5 s
ICU, availability of circulation support – Sustained VT, unstable VT – Bradycardia due to AV block – Torsade de pointes tachycardia or ventricular fibrillation

Baseline characteristics of patients with COVID-19 at the time of admission: (3) Bhatla et al

Characteristic	Overall	Patients in the ICU	Patients in the non-ICU ward	*P**
No. of patients	700	79	621	–
Demographic characteristics				
Age (y)	50 ± 18	63 ± 16	48 ± 18	<.0001
Male	314 (45)	40 (51)	274 (44)	.27
African American	486 (69)	51 (65)	435 (70)	.52
Comorbidities				
Coronary heart disease	76 (11)	21 (27)	55 (9)	<.0001
Heart failure	88 (13)	22 (28)	66 (11)	<.0001
Hypertension	347 (50)	62 (78)	285 (46)	<.0001
Atrial fibrillation history	39 (6)	5 (6)	34 (5)	.79
ICD/PPM	20 (3)	5 (6)	15 (2)	.064
Diabetes mellitus	182 (26)	35 (44)	147 (24)	<.0001
Obstructive sleep apnea	124 (18)	23 (29)	101 (16)	.0048
COPD	63 (9)	14 (18)	49 (8)	.0040
Liver disease	67 (10)	14 (18)	53 (9)	.0089
Chronic kidney disease	80 (11)	16 (20)	64 (10)	.0089
Current tobacco	51 (7)	4 (5)	47 (8)	.49
Admission profile				
Temperature (°F)	98.6 ± 1.0	98.9 ± 1.6	98.6 ± 0.9	.14
Oxygen saturation on presentation (%)	92.2 ± 11.7	89.4 ± 10.3	92.5 ± 12.0	.0006
BMI (kg/m^2)	31 ± 9	33 ± 12	31 ± 8	.14
Baseline laboratory values				
WBC count (cells/μL)	7.3 ± 3.9	9.9 ± 6.3	6.9 ± 3.2	<.0001
Potassium concentration (mmol/L)	4.1 ± 0.5	4.3 ± 0.8	4.0 ± 0.5	.0178
Magnesium concentration (mmol/L)	1.9 ± 0.4	2.1 ± 0.5	1.9 ± 0.3	.0992
Nonelevated troponin concentration†	291 (78)	44 (62)	247 (82)	.0003
BNP concentration (pg/mL)	2940 ± 7962	5347 ± 10381	2214 ± 6950	<.0001
D-dimer concentration (ng/mL)	3.3 ± 10.9	7.2 ± 21.1	2.2 ± 5.1	.0005
Procalcitonin concentration (ng/mL)	1.7 ± 9.9	2.8 ± 10.8	1.4 ± 9.6	<.0001
High-sensitivity CRP concentration (mg/L)	85.3 ± 55.3	112.3 ± 52.1	75.1 ± 53.1	<.0001
Medications during hospitalization				
Hydroxychloroquine	172 (25)	53 (67)	119 (19)	<.0001
Remdesivir	57 (8)	20 (25)	37 (6)	<.0001

Values are presented as mean ± SD or as n (%).

BMI = body mass index; BNP = B-type natriuretic peptide; COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease 2019; CRP = C-reactive protein; ICD = implantable cardioverter-defibrillator; ICU = intensive care unit; PPM = permanent pacemaker; WBC = white blood cell.

**P*-value comparisons for patients in the ICU vs those in the non-ICU ward.

†*Nonelevated troponin concentration on admission* is defined as <0.010 ng/mL. There were 373 patients, who had troponin measured at admission.

Characteristics of cardiac arrests in patients with COVID-19:(3)

Patient no.	Cardiac arrest on hospital day no.	Cardiac arrest rhythm	Background/etiology	Outcome
1	1	Asystole	85 yo nursing home resident presenting with respiratory distress.	ROSC; eventually WOC
2	5	PEA	59 yo with a h/o systemic scleroderma and recent hospitalization for ILD presented with pneumonia and hypoxia.	ROSC; remains hospitalized
3	2	PEA	35 yo who underwent elective C-section and was diagnosed with COVID-19 per routine screening. Suspected amniotic fluid embolism.	ROSC; discharged with baby
4	18	PEA	41 yo with a h/o obesity, CHD, and diabetes presented with respiratory distress.	ROSC; remains hospitalized
5	5	PEA	55 yo with mitral valve endocarditis and developed acute stroke. Recovering from mechanical thrombectomy and became nonresponsive.	Deceased
6	5	PEA	50 yo with a h/o scleroderma after double lung transplantation 2.5 y ago presented with respiratory failure.	Deceased
7	45	Asystole	74 yo presented with respiratory failure. Complicated hospitalization including multiorgan dysfunction.	Deceased
8	1	TdP	42 yo presented with respiratory failure. Complicated hospitalization including left ventricular dysfunction and ECMO.	ROSC; remains hospitalized
9	1	PEA	43 yo with a h/o morbid obesity presented with fever and respiratory distress.	ROSC; discharged

CHD = coronary heart disease; COVID-19 = coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; h/o = history of; ILD = interstitial lung disease; PEA = pulseless electrical activity; ROSC = return of spontaneous circulation; TdP = torsades de pointes; WOC = withdrawal of care; yo = years old.

Post-vaccination cardiac arrhythmia : (4,6,7,11,13,14)

Baseline demographic characteristics of people receiving either ChAdOx1, BNT162b2 or mRNA-1273 vaccines or testing positive for SARS-CoV-2 virus (before or after vaccination), in England between 1 December 2020 and 24 August 2021. Data are presented as column % (counts)

	ChAdOx1	BNT162b2	mRNA-1273	ChAdOx1	BNT162b2	mRNA-1273	Positive SARS-CoV-2 test (amongst total vaccinated)
	One dose (at least) (n = 38,615,491)			Two doses (n = 32,095,748)			
Total number of people	20,615,911	16,993,389	1,006,191	19,754,224	11,972,733	368,791	3,028,867
Sex							
Women	43.3 (8,918,403)	42.6 (7,233,091)	29.9 (300,567)	43.3 (8,559,325)	47.2 (5,650,542)	33.9 (125,120)	45.7 (1,385,137)
Men	34.9 (7,191,428)	31.8 (5,401,842)	28.5 (286,893)	34.9 (6,900,964)	32.6 (3,906,666)	26.4 (97,524)	32.2 (974,389)
Not recorded	21.9 (4,506,080)	25.6 (4,358,456)	41.6 (418,731)	21.7 (4,293,935)	20.2 (2,415,525)	39.6 (146,147)	22.1 (669,341)
Age							
Mean age (s.d.)	55.2 (14.8)	47.8 (21.7)	32.3 (9.4)	55.4 (14.7)	55.5 (20.4)	39.6 (7.3)	44.5 (17.8)
16–29 years	5.2 (1,064,443)	25.2 (4,285,600)	41.4 (416,982)	5.0 (988,291)	10.4 (1,244,710)	6.9 (25,382)	24.4 (738,170)
30–39 years	7.8 (1,598,406)	23.2 (3,945,405)	36.4 (366,327)	7.6 (1,494,285)	20.7 (2,475,091)	43.8 (161,412)	19.0 (574,710)
40+ years	87.1 (17,953,062)	51.6 (8,762,384)	21.2 (222,882)	87.4 (17,271,648)	68.9 (8,252,932)	49.3 (181,997)	56.6 (1,715,987)

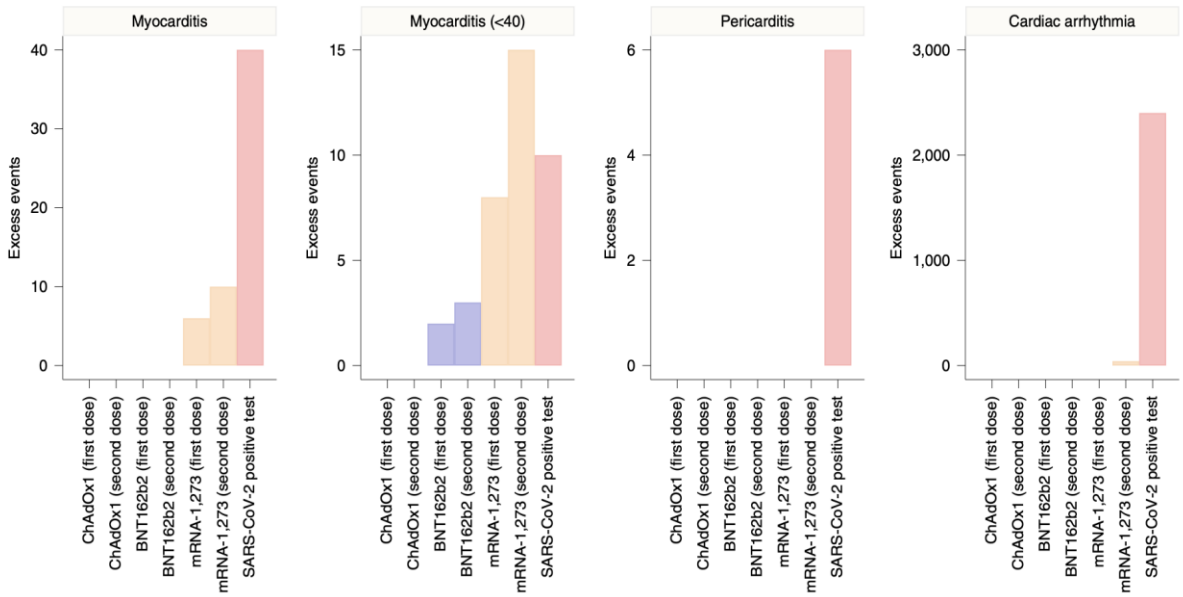
Post vaccination cardiac arrhythmia : (4,7,11,14)

Cardiac inflammation in the previous 2 years[a]							
Previous myocarditis	<0.1 (1,840)	<0.1 (1,485)	<0.1 (56)	<0.1 (1,747)	<0.1 (1,220)	<0.1 (15)	<0.1 (451)
Previous pericarditis	<0.1 (1,849)	<0.1 (1,508)	<0.1 (31)	<0.1 (1,771)	<0.1 (1,285)	<0.1 (8)	<0.1 (346)
Previous cardiac arrhythmia	2.6 (538,564)	2.9 (500,295)	0.3 (2,969)	2.6 (505,794)	3.9 (466,724)	0.3 (1,005)	3.1 (92,985)

Cardiac complication after covid-19 vaccination. (6,7,11,12,14)

Cardiac arrhythmias are more common in patients who have a positive PCR test compared to vaccinated patients.

Number of excess events in the 1–28 days postvaccination/SARS-CoV-2 positive test per 1 million vaccinated/infected.



Demographic characteristics of persons who were infected with SARS-CoV-2 or received a first, second, unspecified, or any dose of an mRNA COVID-19 vaccine* — National Patient-Centered Clinical Research Network, United States, January 1, 2021–January 31, 2022

	No. (%)				
		mRNA COVID-19 vaccination cohort			
Characteristic	SARS-CoV-2 infection cohort†	First dose*,§	Second dose*,§	Unspecified dose*,¶	Any dose*,**
Cohort total	**814,524 (100)**	**2,548,334 (100)**	**2,483,597 (100)**	**1,681,169 (100)**	**6,713,100 (100)**
Age group, yrs					
5–11	76,960 (9)	48,986 (2)	41,742 (2)	30,199 (2)	120,927 (2)
12–17	70,336 (9)	190,810 (7)	179,612 (7)	113,775 (7)	484,197 (7)
18–29	151,950 (19)	308,892 (12)	297,560 (12)	241,787 (14)	848,239 (13)
30–50	255,103 (31)	665,876 (26)	652,947 (26)	490,808 (29)	1,809,631 (27)
51–65	152,243 (19)	601,615 (24)	588,873 (24)	404,445 (24)	1,594,933 (24)
≥66	107,932 (13)	732,155 (29)	722,863 (29)	400,155 (24)	1,855,173 (28)
Sex					
Female	457,506 (56)	1,497,984 (59)	1,463,746 (59)	997,741 (59)	3,959,471 (59)
Male	357,018 (44)	1,050,350 (41)	1,019,851 (41)	683,428 (41)	2,753,629 (41)
Race/Ethnicity††					
Hispanic	133,784 (16)	309,468 (12)	298,270 (12)	169,688 (10)	777,426 (12)
Asian	23,684 (3)	133,445 (5)	131,205 (5)	83,937 (5)	348,587 (5)
Black or African American	162,434 (20)	408,657 (16)	395,283 (16)	283,534 (17)	1,087,474 (16)
Other	34,473 (4)	93,100 (4)	90,122 (4)	54,305 (3)	237,527 (4)
White	408,152 (50)	1,441,573 (57)	1,407,974 (57)	1,001,686 (60)	3,851,233 (57)
Missing§§	58,980 (7)	205,834 (8)	204,224 (8)	98,299 (6)	508,357 (8)

* In the first and second dose cohorts, 27% of persons received mRNA-1273 (Moderna) vaccine and 73% received BNT162b2 (Pfizer-BioNTech) vaccine. In the unspecified dose cohort, 36% received Moderna and 64% Pfizer-BioNTech. In the any dose cohort, 29% received Moderna and 71% Pfizer-BioNTech.
† Persons in the infection cohort included those who received ≥1 positive SARS-CoV-2 molecular or antigen test result.
§ The first dose cohort included persons who had either the first of 2 doses ≥20 days before a second dose or a specific code for a first dose; the second dose cohort included persons who had either the second of 2 doses ≥20 days after a first dose or a specific code for a second dose.
¶ The unspecified dose cohort included persons who had a single dose that was not specified as a first or second dose; doses specified as booster doses were excluded.
** The any dose cohort is the first, second, and unspecified dose cohorts combined; persons who had 2 doses are represented twice in the cohort but had different index dates for their first and second doses.
†† Persons of Hispanic origin could be of any race; Asian, Black or African American, White, or other (which includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiple race, and other race) persons are not Hispanic.
§§ Missing race category includes no information, refused to answer, unknown, or missing.

Arrhythmia associated with Covid-19 medication :(24,38,39,45,51,52)

The treatments that have been used to treat Covid-19 have caused rhythmic side effects by lengthening the QT interval to more than 500ms.

Antiobiotics and antiretrovirals

Drugs	Class	Arrhythmia risk
Remedesivir	Antiviral	Severe hypotension and cardiac arrest[31]
Favipiravir	Antiviral	QTc-interval prolongation in an Ebola-infected patient[32]
Lopinavir/Ritonavir	Anti-retroviral	AV block, PR, QRS, and QTc-interval prolongations[33 34]
Hydroxychloroquine	Antimalarial, immunosuppressant	QTc prolongation, TdP, polymorphic VT/VF[35]
Azithromycin	Macrolide antibiotic	QTc prolongation, TdP, polymorphic VT/VF[36]

AV atrioventricular, QTc heart rate corrected QT interval, TdP torsades de pointes, VF ventricular fibrillation, VT ventricular tachycardia.

Management of arrhythmias: (16,18,19,20)

The management of cardiac arrhythmias linked to covid 19 is no different from those in patients without covid. There are, however, a few additional means to consider:

- Treatment of hypoxemia.

- Treatment of fever.

- Treatment of electrolyte disorders related to vomiting and diarrhea.

- Consider antibiotic treatment responsible for QT prolongation.

- Specific considerations for management cardiac arrhythmia :

  - Rate control for management minimise the risck of QTc prolongation.
  - Implantation temporary pace maker for bradycardie or atrioventricular block.
  - External electric shock sometimes ciculatory assitance (ECMO) to better oxygenate the patient and put the heart at rest.
  - The medical treatment is the same as for non-Covid.

Management considerations for arrhythmias reported in COVID-19 infection:(24,38,39,45,51,52)

Arrhythmia	Primary management considerations
Atrial fibrillation, atrial flutter	• Rhythm or rate control and anticoagulation in patients who meet criteria where benefits may outweigh possible risks • Cardioversion • Ablation when stable and as appropriate
Supraventricular tachycardia	• Rate control • Ablation when stable and as appropriate
Ventricular tachycardia, ventricular fibrillation	• Antiarrhythmics, beta blockers, sedation as appropriate • Avoid QT prolongation; replenish electrolytes and consider ablation and/or ICD implantation when stable/appropriate
Bradyarrhythmia	• Avoid agents that may cause bradycardia • Myocarditis should be considered a possible cause of bradycardia • Consider temporary venous pacemaker or IV dopamine/atropine • Pacemaker implantation when stable and as appropriate
Postural orthostatic tachycardia syndrome (POTS), inappropriate sinus tachycardia (IST)	• Oral hydration • Compression stockings • Beta blockers, possible consideration of off-label use of ivabradine • Cardiac rehabilitation
QT prolongation	• Avoid QT-prolonging agents, replenish electrolytes, closely monitor ECG

ECG = electrocardiogram; ICD = implantable cardioverter-defibrillator; IV = intravenous.

Conclusion

- Heart rhythm disorders are common in infection with the covid 19 virus.
- There mechanism is multifactorial.
- Their prognosis is poor with a high mortality rate testifying to the seriousness of the infection.
- Their management is the same apart from a few considerations.

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