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## CLINICAL RESEARCH

# Care management and 90-day post discharge mortality in patients hospitalized for myocardial infarction and COVID-19: A French nationwide observational study

*Prise en charge et mortalité à 90 jours des patients hospitalisés pour infarctus du myocarde et COVID-19 : une étude observationnelle nationale française*

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### KEYWORDS

Myocardial infarction;  
 COVID-19;  
 Hospitalization;  
 Mortality

### Summary

**Background.** – Concomitant or cured coronavirus disease 2019 (COVID-19) in patients with myocardial infarction (MI) may lead to difficulties in acute care management and impair prognosis.

**Aims.** – To describe and compare the characteristics, care management and 90-day post discharge outcomes of patients hospitalized for MI who did not have COVID-19 with those of patients with concomitant or previous hospital-diagnosed COVID-19.

**Abbreviations:** CABG, coronary artery bypass graft; CI, confidence interval; COVID-19, coronavirus disease 2019; ICD-10, International Classification of Diseases, Tenth Revision; ICU, intensive care unit; MI, myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; SAPSII, simplified acute physiology score; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SNDS, Système National des Données de Santé (French National Health Data System); STEMI, ST-segment elevation myocardial infarction.

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**Methods.** – This population-based French study included all patients hospitalized for MI in France (30 December 2019 to 04 October 2020) from the French National Health Data System. Outcomes were described for each COVID-19 group and compared using adjusted logistic regression analysis.

**Results.** – Among 55,524 patients hospitalized for MI, 135 had previous hospital-diagnosed COVID-19 and 329 had concomitant COVID-19. Patients with previous hospital-diagnosed COVID-19 had more personal history of cardiovascular diseases than those without concomitant/previous confirmed COVID-19. In-hospital and 90-day post discharge mortality rates of patients with previous COVID-19 were 8.1% and 4.0%, respectively, compared with 3.5% and 3.0% in patients without concomitant/previous confirmed COVID-19 (odds ratio [OR]<sub>adj in-hospital</sub> 1.83, 95% confidence interval [CI] 0.97–3.46; OR<sub>adj post discharge</sub> 0.77, 95% CI 0.28–2.13). Patients with concomitant COVID-19 had more personal history of cardiovascular diseases, but also a poorer prognosis than their no concomitant/no previous confirmed COVID-19 counterparts; they presented excess cardiac complications during hospitalization (OR<sub>adj</sub> 1.62, 95% CI 1.29–2.04), in-hospital mortality (OR<sub>adj</sub> 3.31, 95% CI 2.32–4.72) and 90-day post discharge mortality (OR<sub>adj</sub> 2.09, 95% CI 1.24–3.51).

**Conclusions.** – In-hospital and 90-day post discharge mortality of patients hospitalized for MI who had previous hospital-diagnosed COVID-19 did not seem to differ from those hospitalized for MI alone. Conversely, concomitant COVID-19 and MI carried a poorer prognosis extending beyond the hospital stay. Special attention should be given to patients with simultaneous COVID-19 and MI, in terms of acute care and secondary prevention.

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## MOTS CLÉS

Infarctus du myocarde ;  
COVID-19 ;  
Hospitalisation ;  
Mortalité

## Résumé

**Contexte.** – La COVID-19 guérie ou concomitante peut rendre difficile la prise en charge des patients présentant un infarctus du myocarde (IDM) et peut altérer leur pronostic.

**Objectifs.** – Décrire et comparer les caractéristiques, la prise en charge et les résultats 90 jours après la sortie de l'hôpital des patients admis pour un IDM qui n'avaient pas de COVID-19 avec ceux des patients qui avaient une COVID-19 concomitante ou lors d'une précédente hospitalisation.

**Méthodes.** – Cette étude française en population a inclus les données de tous les patients hospitalisés pour un IDM en France entre le 30 décembre 2019 et le 04 octobre 2020. Elle a été réalisée à partir des données du Système National des Données de Santé français. Les résultats ont été décrits selon le statut de COVID-19 et comparés par régression logistique ajustée.

**Résultats.** – Parmi les 55 524 patients hospitalisés pour un IDM, 135 avaient eu une hospitalisation antérieure avec un diagnostic de COVID-19, et 329 avaient un diagnostic de COVID-19 concomitant. Les patients avec un antécédent d'hospitalisation COVID-19 présentaient plus d'antécédents personnels de maladies cardiovasculaires que les patients sans COVID-19 confirmé. La mortalité hospitalière et 90 jours après la sortie de l'hôpital des patients avec antécédents d'hospitalisation COVID-19 étaient, respectivement, de 8,1 % et 4,0 %, comparé à 3,5 % et 3,0 % chez les patients sans COVID-19 confirmé (antécédent ou concomitant) (OR<sub>aj hospitalière</sub> 1,83, IC95 % 0,97–3,46 ; OR<sub>aj 90 jours après la sortie</sub> 0,77, IC95 % 0,28–2,13). Les patients présentant une COVID-19 concomitante à leur hospitalisation pour IDM avaient plus de d'antécédents personnels de maladies cardiovasculaires, mais également un moins bon pronostic que les patients sans COVID-19 confirmé. Ils présentaient plus de complications cardiaques durant l'hospitalisation (OR<sub>aj</sub> 1,62, IC95 % 1,29–2,04). Leur mortalité hospitalière et la mortalité 90 jours suivant la sortie de l'hôpital étaient plus élevées (OR<sub>aj hospitalière</sub> 3,31, IC95 % 2,32–4,72 ; OR<sub>aj 90 jours après la sortie</sub> 2,09, IC95 % 1,24–3,51).

**Conclusions.** – La mortalité hospitalière et la mortalité 90 jours après la sortie d'hospitalisation pour IDM des patients hospitalisés pour IDM avec un antécédent d'hospitalisation COVID-19 ne semblaient pas différer de celles des patients hospitalisés pour un IDM seul dans cette étude. À l'inverse, la présence concomitante de COVID-19 lors d'un IDM entraînait un pronostic plus défavorable des patients, qui s'étendait au-delà du séjour hospitalier. Une attention particulière devrait être apportée aux patients présentant simultanément une COVID-19 et un IDM, tant en termes de prise en charge aiguë que de prévention secondaire.

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## Background

The coronavirus disease 2019 (COVID-19) pandemic has continued to spread since December 2019, and has caused significant mortality worldwide [1]. Patients with underlying cardiovascular disease or cardiovascular risk factors are more likely to be hospitalized for COVID-19, to have a severe form of the disease and to die from it [2,3].

COVID-19 has many complex cardiovascular manifestations, including multiple pathophysiological processes, inflammation and disorders in the coagulation system leading to microthrombi and thromboembolism. Patients with COVID-19 can also present with troponin elevation, with or without ST-segment elevation, related to increased myocardial oxygen demand, with single or multivessel lesions, coronary artery spasm or rupture of atherosclerotic plaque; sometimes, no lesion is seen on coronary angiography [4–7].

Co-existing myocardial infarction (MI) and COVID-19 may lead to difficulties in managing patients, and specific care might be required. Several case series and investigations with small study populations previously highlighted that patients with ST-segment elevation myocardial infarction (STEMI) with concomitant COVID-19 had a poor prognosis, and hospital mortality rates exceeded 10% [8–12]. However, these studies had limited power and were restricted to hospital-based medical outcomes. In addition, the prognosis of patients who have an MI in the weeks following a COVID-19 diagnosis has not been studied. Finally, to the best of our knowledge, no large study to date has assessed how concomitant COVID-19 may impact medium-term outcome following discharge, a period of increased risk for patients with acute MI.

In France, the first cases of COVID-19 were confirmed on 24 January 2020 [13]. The pandemic then spread rapidly, with two waves in 2020 (peaking in March and October, respectively), interrupted by a short-lived improvement during the summer. Of 67 million inhabitants in France, more than 650,000 confirmed cases were reported in early October 2020, and nearly 130,000 hospitalizations [14]. In early 2020, the COVID-19 pandemic significantly affected the French healthcare system, both in- and out-of-hospital care, and there has been a decrease in hospital and emergency department admissions for STEMI [15,16], as well as a change in the management of STEMI [17].

The aim of this nationwide study was to describe the characteristics, acute hospital care management, cardiac complications, in-hospital mortality, 90-day post discharge mortality, hospital readmission rates and post discharge medical follow-up outcomes of patients with MI hospitalized in cardiac intensive care units (ICUs) in France who had concomitant or previous hospital-diagnosed COVID-19, and to compare these data with those for patients hospitalized for MI with no concomitant/previous confirmed COVID-19.

## Methods

### Data source and study population

This study was performed using data from the French National Health Data System (Système National des Données de Santé [SNDS]), which contains comprehensive data

on health insurance claims and hospital discharges for the entire French population (universal coverage) [18]. All patients hospitalized for an MI in France between 30 December 2019 and 04 October 2020, who were admitted to a cardiac ICU, were selected. MI hospitalizations were defined as hospitalizations where the principal diagnosis in at least one medical unit had codes I21, I22 or I23 according to the International Classification of Diseases, Tenth Revision (ICD-10). For each patient, we selected the first hospitalization for MI that occurred during the study period.

### Data collection

All the data used for this study were taken from the SNDS. COVID-19 diagnosis was identified by a primary or associated hospital diagnosis of COVID-19 confirmed either biologically (codes U0710, U0712 and U0714) or by computed tomography scan (U0711). Patients with previous hospital-diagnosed COVID-19 had a COVID-19 code during a hospitalization in 2020, before MI hospitalization (group A). Patients classified as having concomitant MI/COVID-19 only had a COVID-19 code during MI hospitalization (group B). Patients hospitalized for MI who had no history of previous hospital-diagnosed COVID-19 or concomitant confirmed COVID-19 constituted the control group.

Data collected on patients' characteristics and clinical management included age, sex, the Charlson Comorbidity Index score [19], cardiovascular risk factors and personal history of cardiovascular diseases (acute coronary syndrome, ischaemic heart disease, stroke, heart failure, rhythm and conduction disorders, valvular heart disease, venous thrombosis and pulmonary embolism, hypertension, all circulatory diseases, obesity and tobacco consumption), cardiac complications (cardiogenic shock, cardiac rupture, cardiac thrombosis, atrial fibrillation, heart failure, rhythm and conduction disorders, valvulopathy, venous thrombosis and pulmonary embolism), length of stay, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), admission to a resuscitation unit – age and severity score (simplified acute physiology score [SAPSII] [20]) – and the place where patients were discharged to (e.g. home, rehabilitation unit, etc.).

Data on personal history of cardiovascular diseases diagnosed during any hospitalization in the 5 years preceding the MI hospitalization were also extracted. All health reimbursement data for patients with cardiovascular long-term disease status (a specific health status in France whereby all care is reimbursed by the health insurance) were collected, except for hypertension. Hypertension and diabetes were identified from reimbursement for antihypertensive and antidiabetic treatments, respectively. Obesity was estimated from related hospitalizations and bariatric surgery. Tobacco consumption was identified from reimbursements for cessation treatment and related hospitalizations. Cardiac complications were identified using "associated diagnosis" codes during the MI hospitalization. Drug treatments (antihypertensive drugs, statins, antiplatelet agents, nitrates, oral anticoagulants, anti-arrhythmic drugs and antidiabetic drugs) with at least three refunds in the 12 months preceding the MI hospitalization were identified in the database.

Rehospitalizations (with at least 1 night's stay), day-care hospitalization, treatment delivery (at least one refund), medical visits and admission to rehabilitation units within 90 days of discharge from hospital were identified for patients who returned home. Ninety-day post discharge all-cause mortality was estimated for people covered by France's general health insurance scheme (which covers approximately 76% of the French population). Data on date of death are exhaustive and rapidly recorded for this scheme in the SNDS. The 90-day in- and out-of-hospital mortality was all-cause in-hospital and 90-day after discharge mortality.

### Patient consent for publication

In line with French government regulations and the National Ethics Committee's criteria, no patient consent was required. The database used in the study contained anonymous patient information. Furthermore, full access to the SNDS is granted to the National Agency for Public Health (Santé Publique France) by French law (Code de la Santé Publique: articles L. 1461-3 I 2° and R. 1461-12 et seq.).

### Statistical analysis

The characteristics of patients hospitalized for MI were compared between patients who did not have COVID-19, patients with previous hospital-diagnosed COVID-19 and patients with concomitant COVID-19 using either the  $\chi^2$  test or Fisher's exact test, as necessary, for categorical variables, and Student's test for quantitative variables. In-hospital and 90-day post discharge mortality and post discharge medical follow-up outcomes were compared between group A and group B and the controls using multivariable logistic regression analysis adjusted for age, sex, personal history of cardiovascular diseases, obesity, tobacco consumption, diabetes and hypertension. Statistical analyses were performed with SAS software, version 7.11 (SAS Institute Inc., Cary, NC, USA).

## Results

Between 30 December 2019 and 04 October 2020, 55,524 patients were admitted to a cardiac ICU for an MI in France. Among them, 135 patients (0.24%) had previous hospital-diagnosed COVID-19 (group A), with a median time between the COVID-19 hospitalization and the MI hospitalization of 73 days (minimum 1 day; maximum 198 days), whereas 329 others (0.59%) had concomitant COVID-19 (group B), of whom 21% were asymptomatic. A total of 55,060 patients were hospitalized for MI without previous/concomitant confirmed COVID-19 (controls).

### Sociodemographic, medical and hospital characteristics

Patients in groups A and B were older than those in the control group (mean age: 70.7, 68.8 and 66.8 years, respectively) (Table 1). Prevalence of personal history of circulatory diseases was higher in group A than in group B and the control group (88%, 60% and 52%, respectively).

Apart from a lower rate of PCI, acute care management for MI did not differ between patients in group A and the

control group. Patients who did not have a PCI or CABG during their MI hospitalization were older and more likely to be women (data not shown). Acute care management was significantly different in group B patients compared with the two other groups; specifically, their length of stay was twice that of the other groups, they had more cardiac complications and their admission rate to a resuscitation unit was four times higher (18.2%). The main diagnosis (48.3% of this group) for their admission to a resuscitation unit was respiratory disease or associated symptoms.

The in-hospital mortality rate in patients in group A was significantly higher than in the control group (8.1% vs. 3.5%;  $P=0.008$ ), but was not statistically significant after controlling for age, sex, personal history of cardiovascular diseases and cardiovascular risk factors (odds ratio [OR]<sub>adj</sub> 1.83, 95% confidence interval [CI] 0.97–3.46;  $P=0.06$ ). The in-hospital mortality rate in group B was three times higher than in the control group (11.9% vs. 3.5%;  $P<0.0001$ ), and statistically significantly higher after adjustment for age, sex, personal history of cardiovascular diseases and cardiovascular risk factors (OR<sub>adj</sub> 3.31, 95% CI 2.32–4.72;  $P<0.0001$ ) (Fig. 1; Table A.1). Among patients with MI admitted to a resuscitation unit, the in-hospital mortality rate ranged from 17% (control group) to 33% (group A); these rates were not significantly different ( $P=0.22$ ) (Fig. 1; Table A.1).

### 90-day post discharge mortality rate and follow-up

The all-cause 90-day post discharge mortality rate for patients discharged alive from hospital was 3.0% for patients in the control group, 4.0% for those in group A and 7.5% for those in group B (Table 1). After adjustment for age, sex, personal history of cardiovascular diseases and cardiovascular risk factors, the 90-day post discharge mortality rate in group B was significantly higher than in the control group (OR<sub>adj</sub> 2.09, 95% CI 1.24–3.51;  $P=0.006$ ) (Fig. 1; Table A.1).

In total, the 90-day in- and out- of hospital mortality rate was 6.3% in the control group, 10.2% in group A and 18.4% in group B (Table A.1). After adjustment for age, sex, personal history of cardiovascular diseases and cardiovascular risk factors, this mortality rate was three-fold higher in group B than in control group (OR<sub>adj</sub> 2.93, 95% CI 2.08–4.13;  $P<0.0001$ ), but was not significantly different between group A and the control group (OR<sub>adj</sub> 1.07, 95% CI 0.56–2.04;  $P=0.84$ ). A quarter of patients (23.3%) went to a rehabilitation unit directly or within 3 months after their MI hospitalization ended, 80% of these going to a rehabilitation unit specialized in cardiovascular care. Patients in groups A and B were more likely to be referred directly to rehabilitation after their MI hospitalization (14.5% and 12.1%, respectively, with 5.7% for the control group;  $P<0.0001$ ). After controlling for age, sex, personal history of cardiovascular diseases and cardiovascular risk factors, patients in group A were more likely to go to rehabilitation units (OR<sub>adj</sub> 1.76, 95% CI 1.22–2.55;  $P=0.003$ ); these units were more likely to be polyvalent or polypathological hospitals for the elderly. Patients in group A did not go more frequently to rehabilitation units specialized in cardiovascular care (OR<sub>adj</sub> 0.83, 95% CI 0.48–1.43;  $P=0.50$ ), and patients in group B

**Table 1** Description of the characteristics of patients hospitalized for myocardial infarction in France between 30 December 2019 and 04 October 2020, and hospital outcomes, according to COVID-19 status (total  $n = 55,524$ ).

	Control group <sup>a</sup> ( $n = 55,060$ ; 99.16%)	Group A <sup>b</sup> ( $n = 135$ ; 0.24%)	$P_{\text{control-A}}$	Group B <sup>c</sup> ( $n = 329$ ; 0.59%)	$P_{\text{control-B}}$	$P_{\text{B-A}}$
Women	26.7	29.3	0.51	31.6	0.35	0.29
Age (years)	66.8 ± 13.4	70.7 ± 13.3	0.001	68.8 ± 14.3	0.009	0.174
Charlson index ≥ 2	48.4	74.8	< 0.0001	61.7	< 0.0001	0.007
Personal history of CV diseases and risk factors <sup>d</sup>						
Acute coronary syndrome	15.2	28.2	< 0.0001	16.8	0.43	0.0056
Ischaemic heart disease	31.8	55.6	< 0.0001	34.5	0.3073	< 0.0001
Stroke	3.7	10.4	0.001	5.0	0.216	0.033
Heart failure	7.4	31.1	< 0.0001	14.0	< 0.0001	< 0.0001
Rhythm and conduction disorders	12.2	34.1	< 0.0001	18.3	0.0008	0.0003
Valvulopathy	4.6	17.0	< 0.0001	9.9	< 0.0001	0.0333
Venous thrombosis or pulmonary embolism	2.5	8.9	0.0002	5.0	0.0044	0.1109
Pulmonary embolism	1.1	3.7	0.02	1.6	0.41	0.17
Circulatory disease	51.9	88.2	< 0.0001	59.6	0.0059	< 0.0001
Obesity	15.0	23.7	0.01	18.3	0.10	0.19
Tobacco use	34.9	33.3	0.71	31.4	0.19	0.68
Treatments before hospitalization <sup>d</sup>						
Antihypertensive drugs	56.8	77.8	< 0.0001	64.3	0.0065	0.0047
Statins	30.0	45.9	< 0.0001	38.2	0.0014	0.1247
Antiplatelets	31.2	48.9	< 0.0001	39.8	0.001	0.0714
Nitrates	9.5	15.6	0.02	9.6	0.9593	0.0686
Oral anticoagulants	8.5	20.7	< 0.0001	11.2	0.0906	0.0072
Antiarrhythmic drugs	6.9	717.8	< 0.0001	9.6	0.0565	0.0146
Antidiabetic drugs	20.8	42.2	< 0.0001	27.0	0.0059	0.0014
Clinical management						
COVID-19 asymptomatic	—	3.0	—	20.7	—	—
STEMI	53.2	56.3	0.47	55.0	0.51	0.80
Length of stay (days)	6.4 ± 6.3	6.7 ± 6.4	0.49	13.9 ± 14.1	< 0.0001	< 0.0001
PCI	73.5	57.0	< 0.0001	61.4	< 0.0001	0.3835
CABG	2.3	0.7	0.96	3.0	0.38	0.19
Admitted to a resuscitation unit	4.8	4.4	0.86	18.2	< 0.0001	0.00
Simplified acute physiology score (SAPSII) <sup>e</sup>	45.0 ± 22.3	46.3 ± 20.7	0.89	40.3 ± 16.2	0.10	0.40
Age (years) <sup>e</sup>	65.8 ± 11.6	62.2 ± 6.5	0.45	67.4 ± 12.1	0.27	0.12
Complications <sup>f</sup>						
Cardiogenic shock	3.7	4.4	0.65	10.3	< 0.0001	0.04
Cardiac rupture/ventricular septal defect	0.3	0.0		1.2	0.03	
Cardiac thrombosis	0.4	0.7	0.43	0.9	0.16	1.00
Atrial fibrillation and flutter	12.9	18.5	0.05	18.2	0.00	0.94
Rhythm and conduction disorders	28.9	33.3	0.25	36.2	0.00	0.56
Heart failure	22.3	20.7	0.67	38.0	< 0.0001	0.00
Venous thrombosis or pulmonary embolism	1.3	1.5	0.54	3.0	0.01	0.52
Pulmonary embolism	0.3	1.5	0.07	1.8	0.00	1.00

Table 1 (Continued)

	Control group <sup>a</sup>	Group A <sup>b</sup>	$P_{\text{control-A}}$	Group B <sup>c</sup>	$P_{\text{control-B}}$	$P_{\text{B-A}}$
	( <i>n</i> = 55,060; 99.16%)	( <i>n</i> = 135; 0.24%)		( <i>n</i> = 329; 0.59%)		
Place to which patient was discharged <sup>g</sup>						
Home	86.7	71.8	< 0.0001	73.1	< 0.0001	0.78
Rehabilitation unit	5.7	14.5	< 0.0001	12.1	< 0.0001	0.49
Long-term care unit	0.2	1.6	0.0003	1.7	0.0003	0.99
Hospitalization at home	0.1	0.0		0.0		
Psychiatric department	0.1	0.0		0.0		
NA	7.3	12.1	0.04	13.1	0.0001	0.78
Mortality						
In-hospital case fatality	3.5	8.1	0.008	11.9	< 0.0001	0.24
All-cause 90-day post discharge mortality <sup>h</sup>	3.0	4.0	0.55	7.5	< 0.0001	0.22

Data are expressed as % or mean  $\pm$  standard deviation. CABG: coronary artery bypass graft; COVID-19: coronavirus disease 2019; CV: cardiovascular; MI: myocardial infarction; NA: not available; PCI, percutaneous coronary intervention; SAPSII: simplified acute physiology score; STEMI: ST-segment elevation MI.

<sup>a</sup> Did not have confirmed COVID-19 at any time.

<sup>b</sup> Previous hospital-diagnosed COVID-19.

<sup>c</sup> Concomitant COVID-19.

<sup>d</sup> Among those with a unique identifier (54,798 patients = 98.7% of all included patients), hospitalizations or official long-term disease status in the 5 years preceding MI hospitalization.

<sup>e</sup> Among those admitted to a resuscitation unit.

<sup>f</sup> Associated diagnosis during the MI hospitalization.

<sup>g</sup> Among those discharged from hospital alive.

<sup>h</sup> Among those discharged from hospital alive and covered under France's general health insurance scheme.

went less frequently than patients in the control group (OR<sub>adj</sub> 0.63 95% CI 0.44–0.89;  $P=0.01$ ) (Fig. 1; Table A.1).

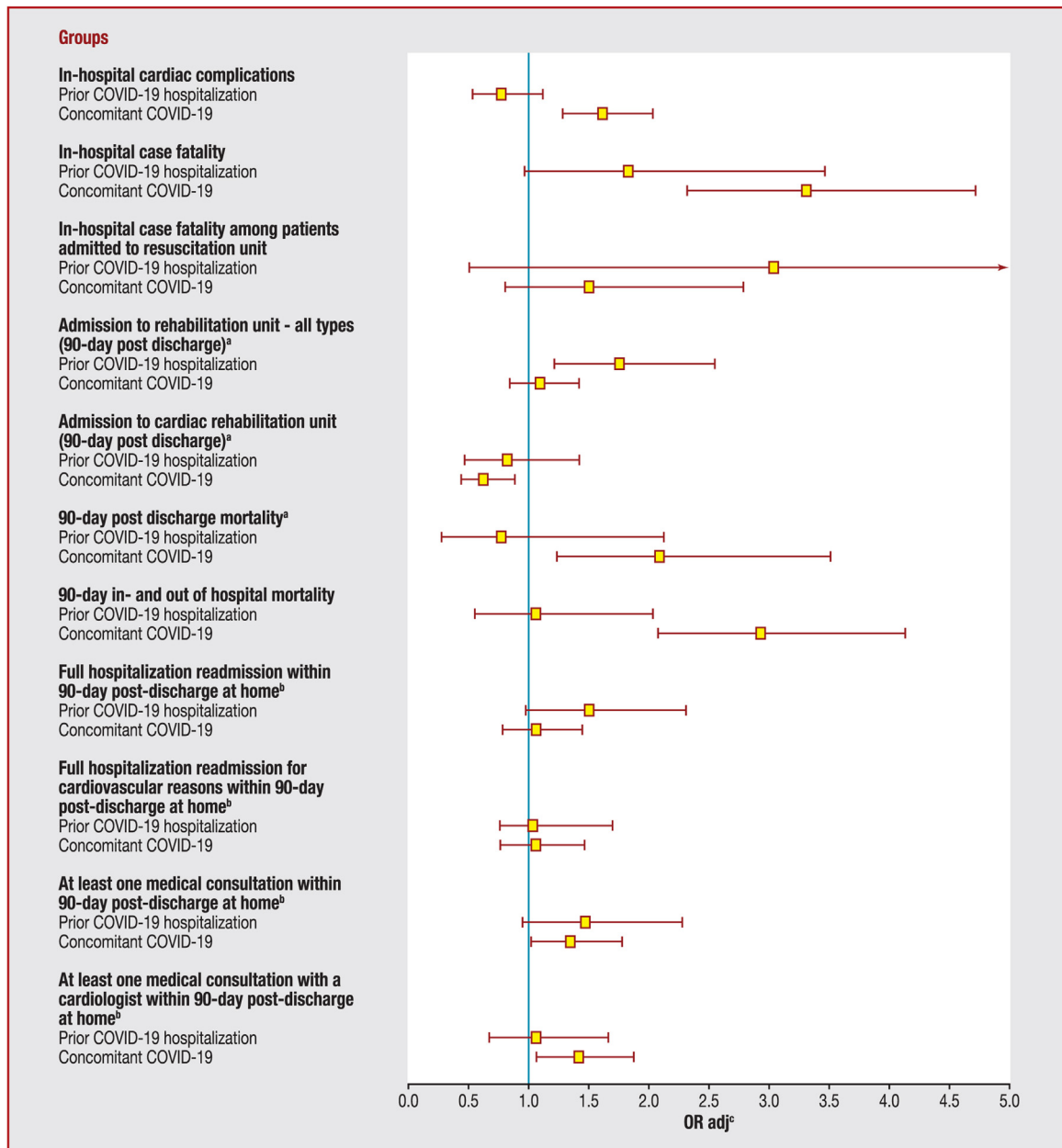
Among patients discharged directly to their homes (86.7% of the control group, 71.8% of group A and 73.1% of group B), over 90% were reimbursed for antihypertensive drugs, statins and antiplatelet agents, and more than 30% had at least one visit with a cardiologist within 90 days of their discharge from the MI hospitalization. Such consultations were more common in group B (39%; OR<sub>adj</sub> 1.42, 95% CI 1.07–1.88;  $P=0.01$ ) (Fig. 1; Table A.1).

Patients in group A were more likely to be readmitted to hospital within 90 days of their discharge than patients in the control group (41.6% vs 27.6%;  $P=0.003$ ) (Table 2), but there was no significant difference in these readmission rates after adjusting for age, sex, personal history of cardiovascular diseases and cardiovascular risk factors (OR<sub>adj</sub> 1.51, 95% CI 0.98–2.31;  $P=0.06$ ) (Fig. 1; Table A.1). No difference was observed in all-cause readmission between group B and the control group (OR<sub>adj</sub> 1.07, 95% CI 0.79–1.45;  $P=0.65$ ). One in five people were readmitted with a primary diagnosis of cardiovascular hospitalization within 90 days of being discharged, with no significant difference between the three groups, even after adjusting for age, sex, personal history of cardiovascular diseases and cardiovascular risk factors. The rates of 90-day post discharge hospital readmission for heart failure varied from 2.5% (control group) to 5.6% (group A) but were not significantly different between the three groups.

## Discussion

In this large French population-based study, we found that previous history of hospital-diagnosed COVID-19 (i.e. before the index acute MI hospitalization) did not seem to have a major impact on in-hospital or post discharge mortality, compared with patients without confirmed COVID-19 history. The concomitant presence of COVID-19 and acute MI, in contrast, was associated with an expected increase in in-hospital mortality, but also with increased 90-day mortality in patients discharged alive, suggesting a prolonged deleterious impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in these patients.

This is the first study to specifically investigate the impact of previous hospital-based COVID-19 diagnosis in patients hospitalized for an MI. These patients were older and had more personal history of cardiovascular diseases than their concomitant counterparts and patients who did not have COVID-19 at any point (control group). The latter finding is not surprising given that older age, obesity, diabetes and cardiac co-morbidities are all risk factors for COVID-19 [2,3]. Consequently, the impact of previous COVID-19 on vital prognosis was marked, with a crude in-hospital mortality rate higher than that in the control group. However, after adjusting for age, sex, personal history of cardiovascular diseases and cardiovascular risk factors, mortality was numerically but not statistically significantly higher. Accordingly, this excess mortality seemed to be related more to patients'



**Figure 1.** Odds ratios (ORs) of in-hospital and 90-day post discharge outcomes of patients hospitalized for myocardial infarction (MI). COVID-19: coronavirus disease 2019. <sup>a</sup>Among patients discharged alive after hospitalization for MI. <sup>b</sup>Among patients discharged to their home after hospitalization for MI. <sup>c</sup>Adjusted for age, sex, history of acute coronary syndrome, stroke, heart failure, rhythm and conduction disorders, valvulopathy, thromboembolism, tobacco consumption, obesity, antihypertensive drugs and antidiabetic drugs.

profiles than to any post COVID-19 effect. The latter result is reassuring as, all co-morbidities being equal, the prognosis of patients with an MI occurring after COVID-19 is cured appears similar to that for patients who did not have the disease at any point. Our results, however, need to be confirmed, as the population of patients with a history of COVID-19 before the index MI hospitalization in our study was not large enough to formally exclude a specific impact of COVID-19. Also, the population size was too limited to analyse outcomes according to the time elapsed between the COVID-19 hospitalization and the MI hospitalization.

As expected, the management of patients with MI seems to be more complex when they have concomitant COVID-19;

we found that these patients had four times the admission rate to resuscitation units and a higher incidence of all cardiac complications than patients with previous COVID-19 diagnosis or those in the control group. The length of stay of patients with MI with concomitant COVID-19 was twice as long as that of patients in the other two groups, and those observed in France for the management of MI [21].

In addition to the specific complications of MI, more venous thrombosis or pulmonary embolism has been observed in patients with COVID-19 concomitantly with MI than in patients with MI with or without a previous history of confirmed COVID-19; this is probably related to the infection itself and, as has been widely demonstrated elsewhere



**Table 2** Description of 90-day outcome and follow-up of patients discharged to their homes after hospitalization for myocardial infarction (total  $n = 45,708$ ).

	Control group <sup>a</sup> ( $n = 45,471$ ; 99.48%)	Group A <sup>b</sup> ( $n = 89$ ; 0.19%)	$P_{\text{control-A}}$	Group B <sup>c</sup> ( $n = 208$ ; 0.46%)	$P_{\text{control-B}}$	$P_{\text{B-A}}$
Drug reimbursement within 90 days of discharge <sup>d</sup>						
Antihypertensive drugs	96.6	94.4	0.24	93.3	0.01	0.72
Statins	92.6	85.4	0.009	87.0	0.002	0.71
Antiplatelet drugs	96.4	88.8	0.002	90.9	< 0.0001	0.58
Nitrates	38.3	30.3	0.12	33.7	0.17	0.58
Oral anticoagulants	14.4	20.2	0.11	20.7	0.01	0.93
Antiarrhythmic drugs	9.4	14.6	0.09	10.1	0.71	0.26
Antidiabetic drugs	22.0	38.2	0.0002	26.4	0.12	0.04
Medical consultation within 90 days of discharge						
At least one medical consultation	52.0	64.0	0.02	60.1	0.02	0.52
At least one consultation with a cardiologist	31.0	32.6	0.75	38.9	0.01	0.30
Readmission to short-stay hospital (medicine, surgery or obstetrics) within 90 days of discharge						
Day-care hospitalization within 90 days of discharge (no overnight stay)	9.2	21.3	0.0006	6.7	0.22	0.0002
Full hospitalization (i.e. with at least 1 night's stay), all reasons	27.6	41.6	0.003	30.3	0.39	0.06
COVID-19	0.4	0.0		0.5	0.52	
CV reasons	20.5	23.6	0.47	22.1	0.57	0.78
Ischaemic heart disease	16.1	13.5	0.50	13.9	0.40	0.99
MI	3.8	5.6	0.39	1.9	0.16	0.13
Heart failure	2.5	5.6	0.08	3.4	0.44	0.35
Pulmonary embolism	0.09	0		0.5		
Rhythm and conduction disorders	1.2	3.4	0.09	2.9	0.04	0.99
Admission to rehabilitation unit within 90 days of discharge						
All rehabilitation units	17.6	16.9	0.86	12.0	0.04	0.26
Cardiac rehabilitation unit	16.2	10.1	0.12	8.7	0.003	0.69
Respiratory rehabilitation unit	0.1	1.1	0.04	0.0		
Polyvalent or polypathology unit for the elderly	1.1	3.4		2.9	0.02	0.99

Data are expressed as % or mean  $\pm$  standard deviation. COVID-19: coronavirus disease 2019; CV: cardiovascular; MI: myocardial infarction.

<sup>a</sup> Did not have confirmed COVID-19 at any time.

<sup>b</sup> Previous hospital-diagnosed COVID-19.

<sup>c</sup> Concomitant COVID-19.

<sup>d</sup> At least one refund.

[22,23], it may alter the patient's prognosis independent of the MI. Changes in the management of patients with COVID-19 have occurred since the beginning of the pandemic, including more frequent full anticoagulation. PCI was used less frequently in both COVID-19 groups (i.e. previous diagnosis and concomitant) than in the control group. This may be explained by several factors. First, patients with no PCI were older than those with PCI. Accordingly, this older population may have different indications for PCI. Second, it may be the result of a different MI pathophysiology in patients with COVID-19. Stefanini et al. reported that up

to 40% of patients with concomitant COVID-19 and STEMI did not have obstructive coronary artery disease identifiable by coronary angiography [7], which may explain why stent placements and PCI were less common in our group B patients. Third, this difference may be caused by difficulties in providing prompt care because of concomitant infection or a history of COVID-19. Fourth, a change in care practices may have occurred at the beginning of the pandemic. During the first months of the COVID-19 pandemic, several studies suggested suboptimal results after primary PCI for patients with concomitant STEMI and COVID-19, because of

hypercoagulability, [24]. Accordingly, fibrinolysis was subsequently used more widely [8,9,25] during this period in concomitant patients, but also in patients with STEMI who did not have COVID-19. Later studies called into question the efficacy of using fibrinolysis for this indication [12,26,27].

Patients in both COVID-19 groups went sooner and more frequently to rehabilitation units than the control group, probably because of the extra care required to manage both cardiac and COVID-19-related respiratory rehabilitation. Moreover, irrespective of age, sex and co-morbidities, patients with previous hospital-diagnosed COVID-19 were more likely to go to poly pathology rehabilitation units, and less likely to go to cardiovascular-specific rehabilitation units, suggesting a need for rehabilitation that goes beyond simply post MI care.

The 90-day post discharge outcomes of patients hospitalized for MI with concomitant COVID-19 are of particular concern, as their prognosis seemed to be strongly affected by the concomitant disease. COVID-19 itself is a risk factor for thromboembolic and cardiac complications [5,28]. High rates of multivessel thrombosis, stent thrombosis and death have been reported elsewhere in patients with STEMI and concomitant COVID-19 [9,10]. In addition, persistence of an inflammatory process in patients with concomitant COVID-19 might increase the risk of further cardiovascular complications in the first months following discharge, a period already known to be at higher risk following an acute coronary syndrome [29–31].

## Strengths and limitations

The key strengths of this study include its population-based nationwide dimension—enabling us to include a rather large number of patients with MI who had concurrent COVID-19—which makes it the largest study on the subject to date; this provided satisfactory statistical power to assess complications and mortality in patients with concomitant MI and COVID-19.

As already pointed out, the main limitation of this study was that it was not possible to establish the temporality between COVID-19 and MI occurrence in the concomitant group. For some people, MI may have been the first manifestation of COVID-19 [7], whereas others may have been infected with SARS-CoV-2 after MI occurrence. It is also important to point out that cardiac complications can occur in patients with COVID-19 even when the disease is not severe [32]. For group A, the time between COVID-19 and MI hospitalization can be variable, but the median time between the two hospitalizations was 73 days, and only 8% of group A patients had a time of less than 1 week between the two hospitalizations.

The proportion of patients with MI with concomitant COVID-19 was highly dependent on the incidence of infection during the year. In January, no patient was infected by SARS-CoV-2 [13], and then the inclusion of January MI cases in the study increased the share of patients in the control group.

The control group may include asymptomatic or mildly symptomatic patients with COVID-19; in fact, patients without biologically or computed tomography-confirmed COVID-19. However, the difference between the groups may be minimized by this classification bias. In addition, given

the size of the no concomitant/previous confirmed COVID-19 group compared with the size of the other groups, the effect of previous or concomitant COVID-19 on the group as a whole is probably limited.

During the COVID-19 pandemic, systematic screening for COVID-19 at hospital admission, regardless of the reason for hospitalization, may have led to the detection of asymptomatic COVID-19 in patients consulted for an MI. Group B may therefore include patients with COVID-19 of differing severities. Restriction of this group to patients with the most severe COVID-19 could increase the difference in mortality and complications found between the control and group B.

Finally, people with a history of COVID-19 (group A) may have been more prone to early detection and management than controls. This bias may have minimized the deleterious effect of previous COVID-19 infection compared with concomitant COVID-19 infection, but this hypothesis is difficult to test with our data.

Another study limitation regards the database used. To limit the problem of miscoding of MI in the principal diagnosis, we selected only patients who were admitted to a cardiac ICU. There may have been coding gaps or errors for associated diagnoses (obesity, smoking, complications). The difference in the filling in of associated diagnoses could lead to increased differences between the groups if they were more frequently reported for patients with confirmed COVID-19 than for those without. Personal history of cardiovascular diseases was identified from previous hospitalizations and long-term disease status, and may therefore be missed if the pathology did not require hospitalization or have long-term status before the MI hospitalization. It is likely that the lack of exhaustiveness of this information is the same regardless of COVID-19 status. Some clinical information may have been missing, such as MI severity and time intervals between the MI symptom onset and coronary angiography. Our database does not support an accurate determination of MI severity on admission to hospital. The rate of cardiac complications can be used to approximate the severity of the MI, but does not indicate the initial condition of the MI. However, we observed the same rate of STEMI between the three groups. The resuscitation rate and SAP-SII show the severity of the MI, but also COVID-19 for group B. The exhaustiveness of PCI or CABG procedures can be discussed, as no study has evaluated the exhaustiveness of this information in the PMSI; however, medicoeconomic use and the comparison of the rates of procedures observed in our study with those of the FAST-MI study [33] seem to show that PCI and CABG are well documented in our database. The information about place of discharge was inaccurate for 6% of patients, possibly because of a wrong coding of the place of discharge or because of a problem with identifiers between stays.

With regard to the latter, if concomitant COVID-19 complicated hospital admission for MI, this time interval may have been longer, leading to increased severity of the MI and therefore the risk of complications. This could be an explanatory factor for the observed differences according to COVID-19 status [6,34]. Further studies on MI registries could provide this information. Also, troponin elevations corresponding to type 2 MIs in patients hospitalized with COVID-19 may not have been coded as MIs.

Finally, data on 90-day post discharge mortality rates were only available for the 76% of the French population covered under France's general health insurance scheme. However, this scheme impacts the whole population equally (i.e. no differential effect according to COVID-19 status).

## Conclusions

Patients hospitalized with MI and concomitant COVID-19 represent a highly vulnerable population during hospitalization, but also after hospitalization discharge. Therefore, optimal secondary prevention and cardiac rehabilitation together with close medical follow-up after hospital discharge are key issues to reduce the burden of complications in these patients.

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The other authors declare that they have no competing interest.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.acvd.2021.11.002>.

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