

Impact of coronavirus disease 2019 (COVID-19) outbreak on acute admissions at the emergency and cardiology departments across Europe



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**Abstract**

**Purpose:** We evaluated whether the severe acute respiratory syndrome coronavirus 2 pandemic was associated with changes in the pattern of acute cardiovascular admissions across European centres.

**Methods:** We set-up a multi-centre, multi-national, pan-European observational registry in 15 centres from 12 countries. All consecutive acute admissions to emergency departments and cardiology departments throughout a 1-month period during the COVID-19 outbreak were compared with an equivalent 1-month period in 2019. The acute admissions to cardiology departments were classified into 5 major categories: acute coronary syndrome, acute heart failure, arrhythmia, pulmonary embolism and other.

**Results:** Data from 54331 patients were collected and analysed. Nine centres provided data on acute admissions to emergency departments comprising 50384 patients: 20226 in 2020 vs 30158 in 2019 – incidence rate ratio (IRR) with 95% confidence interval (95%CI): 0.66(0.58-0.76). The risk of death at the emergency departments was higher in 2020 vs 2019: odds ratio (OR) with 95%CI: 4.1(3.0-5.8),  $P<0.0001$ . All 15 centers provided data on acute cardiology departments admissions: 3007 patients in 2020 vs 4452 in 2019, respectively, IRR(95%CI): 0.68(0.64-0.71). In 2020, there were less admissions with IRR(95%CI): acute coronary syndrome: 0.68(0.63-0.73), acute heart failure: 0.65(0.58-0.74), arrhythmia: 0.66(0.60-0.72), other: 0.68(0.62-0.76); we found a relatively higher percentage of pulmonary embolism admissions in 2020: OR(95%CI): 1.5(1.1-2.1),  $P=0.02$ . Among patients with acute coronary syndrome there were fewer admissions with unstable angina: 0.79(0.66-0.94), non-ST segment elevation myocardial infarction: 0.56(0.50-0.64) and ST-segment elevation myocardial infarction: 0.78(0.68-0.89).

**Conclusion:** In the European centres during the COVID-19 outbreak, there were fewer acute cardiovascular admissions. Also, fewer patients were admitted to the emergency departments with 4-times higher death risk at the emergency departments.

### CLINICAL SIGNIFICANCE

- In the European centres during the COVID-19 outbreak fewer patients were admitted to the emergency departments.
- Patients presented at emergency departments had higher risk of death in 2020 compared with the same period in 2019.
- There was also a significant decrease in acute admissions to the cardiology departments during the COVID-19 outbreak.

- Patients admitted to the cardiology departments were younger and had shorter length of in-hospital stay.

## **Introduction**

Rapid outbreak of new coronavirus disease (COVID-19) has substantially changed the healthcare systems in all countries across the globe, which mainly have focused on pandemic as a state of emergency, according to the declaration of the World Health Organization from January 30<sup>th</sup>, 2020. Strict restrictions have been imposed and millions of people remained at home to minimize SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) transmission. Planned hospital admissions and outpatient visits are either very limited or cancelled<sup>1</sup>. In many countries, there has also been a significant decrease in acute admissions to cardiology departments<sup>2-6</sup>. The limited access to public medical care, fear of infection of SARS-CoV-2 and reorganisation of medical services may have an impact on the number and profile of patients admitted to cardiology departments but also those presenting emergency departments with subsequent changes in the outcomes<sup>7,8,9</sup>. The aim of this study was to present the pan-European data regarding the effects of the COVID-19 pandemic on the pattern of acute cardiovascular admissions across European centres in the countries affected by the disease.

## **METHODS:**

### **Study design**

A multi-centre, multi-national (pan-European) observational registry was set-up. All consecutive acute admissions to the emergency departments and cardiology departments throughout a 1-month period during the COVID-19 outbreak were retrospectively collected. This period differed across participating European countries depending on the “peak month” of SARS-CoV-2 infection at a particular centre (decision which period to select was left at the

discretion of the investigator) but was limited to a period between March 01, 2020 and April 30, 2020. The data was compared with the corresponding period of 1-month in the year 2019. Fifteen centers from 12 countries participated in the registry. All 15 centers delivered data on the acute admissions to the cardiology departments and 9 centres provided data on acute admissions to the emergency departments and subsequently to cardiology departments. The sample size was determined by the time window of the study. The following information was collected in patients presenting to the emergency departments: sex, age, result of reverse transcription-polymerase chain reaction tests from an upper airway swab for SARS-CoV-2 (if available), discharge status (categorized into: admitted to the cardiology departments or discharged/transferred to non-cardiac department or death at the emergency departments. For those admitted to the cardiology departments, we collected additional information on major primary diagnosis which was classified into major 5 categories: acute coronary syndrome, acute heart failure, arrhythmia, pulmonary embolism and other. For several diagnosis in one patient, priority was given for: pulmonary embolism > acute coronary syndrome > acute heart failure > arrhythmia. Other was chosen when none from pre-specified diagnoses was indicated.

The information on length of hospital stay and on in-hospital deaths was also collected. Patients admitted with a diagnosis of acute coronary syndrome were classified as those with unstable angina, non-ST segment elevation myocardial infarction (NSTEMI) or ST-segment elevation myocardial infarction (STEMI); types of arrhythmia admissions included atrial, ventricular, heart blocks/bradycardia. Collecting information about the different categories of acute coronary syndrome and arrhythmia was optional.

Data were retrospectively obtained in individual centres from their own clinical databases using the data-form provided by the coordinating centre (Medical University, Wroclaw, Poland). The final database was double checked for missing or potentially incorrect entries. In



each centre, the principal investigator took full responsibility for the accuracy and quality of the data. The study protocol was approved by the local ethics committee and was conducted in accordance with the Declaration of Helsinki <sup>10</sup>.

Acute coronary syndrome was defined in accordance with the fourth universal definition of myocardial infarction<sup>11</sup>, heart failure was diagnosed based on the guidelines for the diagnosis and treatment of acute and chronic heart failure<sup>12</sup>. Atrial arrhythmias included atrial fibrillation, atrial flutter, tachycardia with narrow QRS and supraventricular tachycardia with wide QRS<sup>13</sup>. Ventricular arrhythmias included ventricular fibrillation and ventricular tachycardia<sup>14</sup>. Bradycardia was recognized when symptomatic, including heart blocks (2<sup>nd</sup> degree, 3<sup>rd</sup> degree block). Pulmonary embolism was confirmed according the guidelines of acute pulmonary embolism <sup>15</sup>.

## Outcomes

The outcomes measures were:

- a. The number of acute admissions to the emergency departments and cardiology departments.
- b. for patients admitted to the emergency departments: death at the emergency departments, transfer to cardiology departments, discharge or transfer to a non-cardiac department.
- c. for patients admitted to the cardiology departments: in-hospital mortality, duration of hospital stay in patients discharged home.

## Statistical Analysis

Normally distributed continuous variables were presented as means  $\pm$  standard deviations.

The intergroup differences were tested using Student's t-test, the Mann-Whitney U test.

Variables with a skewed distribution were expressed as medians with lower and upper quartiles. The categorical variables were expressed as numbers with percentages. The inter-group differences were tested using the  $\chi^2$  test. The associations between death and risk factors were tested using univariable and multivariable logistic regression models. To estimate odds ratios (ORs) with 95% confidence interval (95%CI), a logistic regression was applied with a "successes/failures" matrix to produce the correct binomial denominator. The independent variables were the year of the hospitalization (2019 year as a reference), age  $\geq$  65 years old, male gender, presence of SARS-CoV-2 infection and death was a dependent variable. The multivariable model included variables which were statistically significant associates in univariable models, and remained statistically significant also in a multivariable. To model incidence rate ratio (IRR) and 95%CI between the periods, the negative binomial regression was used. Additionally, in order to compare the estimated IRRs among the study centres, we performed a meta-analysis. Poisson process was involved to figure out the duration of hospitalization (waiting time) in cardiology departments and home discharge. Allowing for greater dispersion or variance of times, the negative binomial distribution was assumed for response data. The difference of duration of hospitalization between 2020 study period and 2019 intra-year control period was expressed by a rate ratio (RR). A value of  $P < 0.05$  was considered as statistically significant. Statistical analysis was performed using the STATISTICA 13.3 data analysis software system (StatSoft, Inc) and in R statistical platform (R Core Team. R: A language and environment for statistical computing (Version 3.6.3. R Foundation for Statistical Computing, Vienna, Austria. 2020) and "metafor", Meta-Analysis Package for R. (Version 2.4-0. CRAN, Austria).

**RESULTS:**

Fifteen cardiac centers from 12 countries participated in the registry and data from 54331 consecutive patients (mean age  $59\pm 20$  years, 51% male) were collected and analysed.

**Patients admitted to the emergency departments***Characteristics, including SARS-CoV-2 status in study group*

Nine centres provided data on acute emergency departments admissions comprising 50384 patients. In total there were 20226 patients admitted to the emergency departments in 2020 vs 30158 in 2019: IRR (95%CI): 0.66 (0.58-0.76). Among patients presented at the emergency departments in 2020 (vs 2019) there were more men: 10748 (53%) vs 14593 (48%) and less patients above 65 years old: 8022 (40%) vs 12994 (43%), all  $P<0.0001$ ; There was no difference in out-of hospital cardiac arrest as cause of admission: 40 (0.24%) vs 46 (0.18%),  $P=0.23$ .

During the study period, 7476 (37%) of all patients were evaluated for the presence of SARS-CoV-2 infection and in 4168 (21%) COVID-19 was confirmed. Those patients were older ( $65\pm 15$  vs  $56\pm 20$  years), and above 65 years old: 2132 (51%) vs 5890 (37%), and were more often males: 2604 (62%) vs 8144 (51%), all  $P<0.0001$ , when compared with patients without suspicion and with negative test for SARS-CoV-2. Moreover, patients with confirmed COVID-19 had lower mortality at emergency departments: 11 (0.26%) vs 119 (0.74%), OR (95%CI) 2.8 (1.5-5.2),  $P<0.001$  and almost all were transferred to non-cardiac departments or discharged: 4111 (99%) vs 14557 (91%),  $P<0.0001$  in comparison to the group without suspicion and with negative test for SARS-CoV-2.

*Outcomes*

The rate of death at the emergency departments was significantly higher in 2020 vs 2019 with 130 (0.64 %) deaths in 2020 vs 48 (0.16%) deaths in 2019 (IRR (95%CI): 2.7 (1.94-3.77),

P<0.0001). In the logistic multivariable regression model for all patients hospitalised at the emergency departments, the year of the hospitalisation 2020, age  $\geq 65$  years old, and male gender were associated with an increased risk of all-cause death (OR (95%CI): 4.1 (3.0-5.8), P<0.0001, 7.1 (4.8-10.5), P<0.0001 and 1.8 (1.3-2.4), P=0.0001, respectively).

The percentage of patients transferred from the emergency departments to the cardiology departments was similar: 1427 (7.1%) vs 2085 (6.9%) (2020 vs 2019, respectively), P=0.54, IRR (95%CI): 0.68 (0.64-0.73).

### **Patients admitted to the cardiology departments**

#### *Characteristics and pattern of clinical diagnoses*

All 15 centers provided data on acute admissions to cardiology departments. There were 3007 patients admitted to cardiology departments in 2020 vs 4452 in 2019, respectively – IRR (95%CI): 0.68 (0.64-0.71).

Patients admitted in 2020 were younger:  $\geq 65$  years 1842 (61%) vs 2871 (64%) in 2020 vs 2019, respectively, P<0.001. There was no difference in gender: males 1928 (64%) vs 2370 (64%), P=0.63. There were less admissions across the following four categories with IRR (95%CI): acute coronary syndrome: IRR (95%CI): 0.68 (0.63-0.73); acute heart failure: 0.65 (0.58-0.74); arrhythmia: 0.66 (0.60-0.72); other: 0.68 (0.62-0.76), all P<0.0001; only for pulmonary embolism there was no difference, IRR (95%CI): 1.00 (0.72-1.39) (Table 1, Figure 1), which resulted in a relatively higher percentage of patients admitted with pulmonary embolism in 2020: 71 (2.4%) in 2020 vs 71 (1.6%) in 2019 (OR (95%CI): 1.49 (1.07-2.08), P=0.02) (Table 2).

There were fewer admissions in all 3 categories of acute coronary syndrome with IRR (95%CI) for unstable angina: 0.79 (0.66-0.94), P<0.01; for NSTEMI: 0.56 (0.50-0.64), P<0.0001; and STEMI: 0.78 (0.68-0.89), P<0.001, respectively. However if analysed as

percentage of all acute coronary syndrome admissions in 2020, unstable angina constituted for 21%, NSTEMI for 41% and STEMI for 37%, whereas in 2019 unstable angina constituted for 18%, NSTEMI for 49% and STEMI for 32% - resulting in a relatively lower percentage of NSTEMI and higher percentage of STEMI in 2020 (Table 3, Figure 2).

There was a reduction in admissions of all 3 groups admitted with a primary diagnosis of arrhythmia: IRR (95%CI) for atrial arrhythmias: 0.69 (0.6-0.77),  $P<0.0001$ ; for ventricular arrhythmias: 0.65 (0.48-0.88),  $P<0.01$ ; and for bradycardia/heart atrioventricular blocks: 0.50 (0.37-0.67),  $P<0.0001$ , respectively. There was a relative decrease in the percentage of bradycardia/heart atrioventricular blocks: 11% in 2020 vs 14% in 2019, OR (95%CI): 0.73 (0.53-1.00),  $P<0.05$ . (Table 4, Figure 3).

#### *Outcomes*

There was no statistically significant difference in death rate between studied periods: 107 (3.6%) in 2020 vs 175 (3.9%) deaths in 2019: OR (95%CI) 0.92 (0.72-1.18),  $P=0.57$ . The mean length of stay was significantly shorter in 2020 in comparison to 2019 ( $4.9\pm 5.0$  vs  $5.9\pm 7.2$ ,  $P<0.0001$ ).

#### **Discussion**

In this pan-European study, we have shown a marked reduction in patients presenting to the emergency departments. In comparison to the last year (2019), these patients were younger, more frequently male, but the most striking finding was the much higher mortality with a 4-times higher death risk at the emergency departments during the COVID-19 outbreak, which was not related to COVID-19 directly. These findings were consistent across all countries/centres, including the 2 centres from the countries that were most severely hit by the pandemic (Madrid/Spain and Bergamo/Italy).

Numerous factors may explain the main finding (“significantly less presentations of patients to the emergency departments /cardiology departments”). One can assume that fear of being easily infected in the hospital precluded many patients to seek medical care. Reorganisation of the health service and focus on fighting the pandemic resulted in difficulties to get access to medical care. Based on the data presented, one can speculate that patients with more advanced/severe cardiovascular disease were admitted to the emergency departments, which resulted in higher risk of death. Another possible cause, may be the allocation of resources, manpower and equipment for younger patients with higher chance of survival. This illustrates a potentially worrying situation once capacities of the healthcare system are being challenged. Additionally, we noted a significant decrease in acute admissions to the cardiology departments – across all European countries - during the COVID-19 pandemic, with a marked reduction in acute cardiovascular admissions due to acute coronary syndrome, acute heart failure and arrhythmias. Of note, only pulmonary embolism was more often present during the COVID-19 outbreak. We showed that the admitted patients were younger, in-hospital stay was shorter and in-hospital mortality was similar compared to the control period (2019). The interesting aspect is shortening of length of stay, due to the possibly modification of therapeutic aims with minimising the hospitalisation time. Moreover, the total number of acute coronary syndrome admissions was reduced by more than 30% (homogenous across all centres), with a reduction in NSTEMI (or unstable angina) but an increase in STEMI. Patients presenting with STEMI are more symptomatic and tend to seek for medical care faster as compared to NSTEMI and unstable angina, which possibly explains these differences. In addition, less physical activity may have masked symptoms. However, less activity may increase the risk of thromboembolism, potentially responsible for the higher percentage of pulmonary embolism, together with COVID-19 incidence. However, this interesting aspect of potential change of health care decisions to possibly earlier change of therapeutic aims.

## Conclusion

This pan-European study shows that during the COVID-19 outbreak, there was a significant decrease in acute admissions to the cardiology departments. Patients admitted were younger, stayed shorter in the hospital, and there was similar in-hospital mortality compared with 2019. Additionally, fewer patients were admitted to the emergency departments with 4-times higher death rate.

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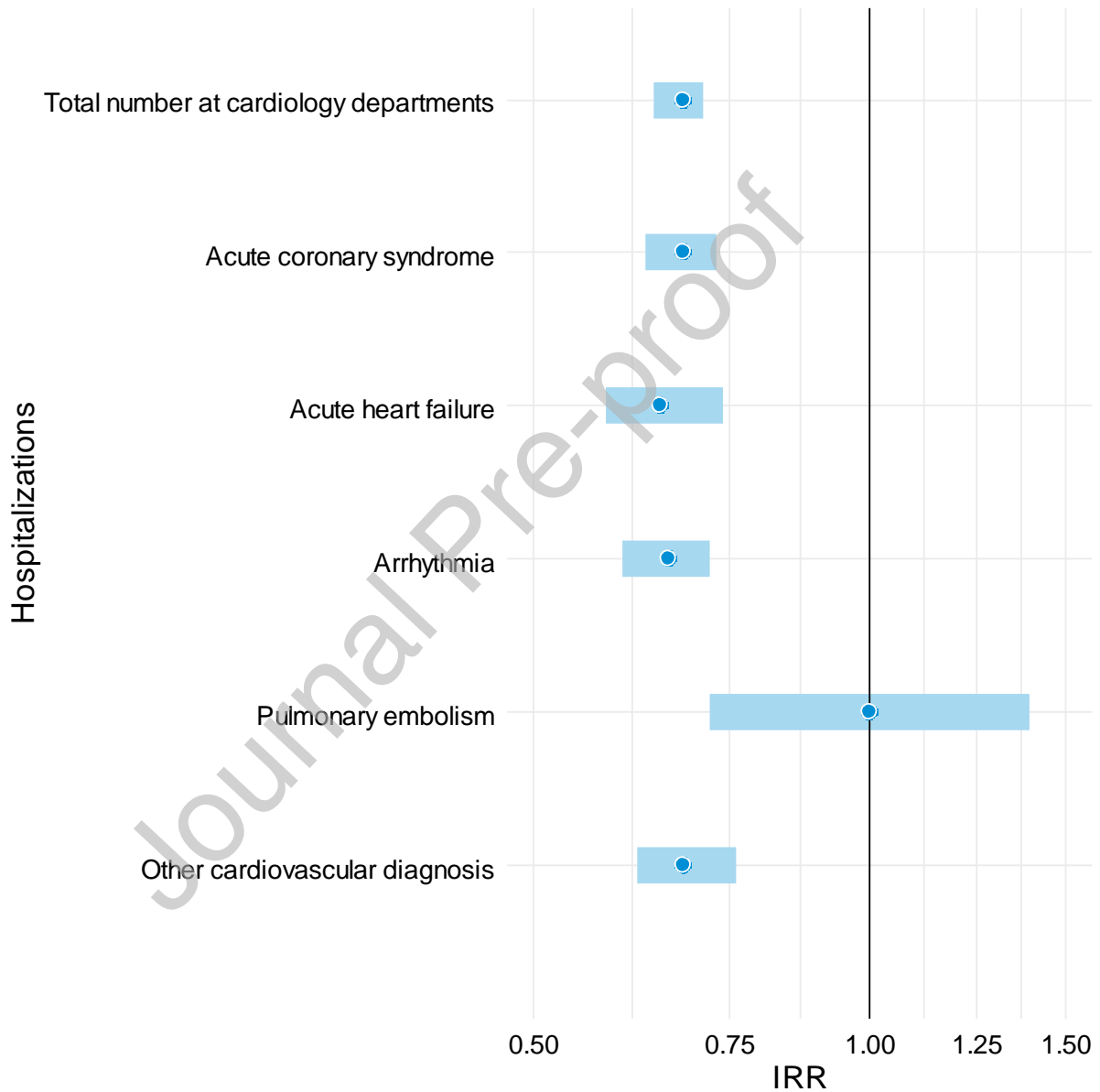
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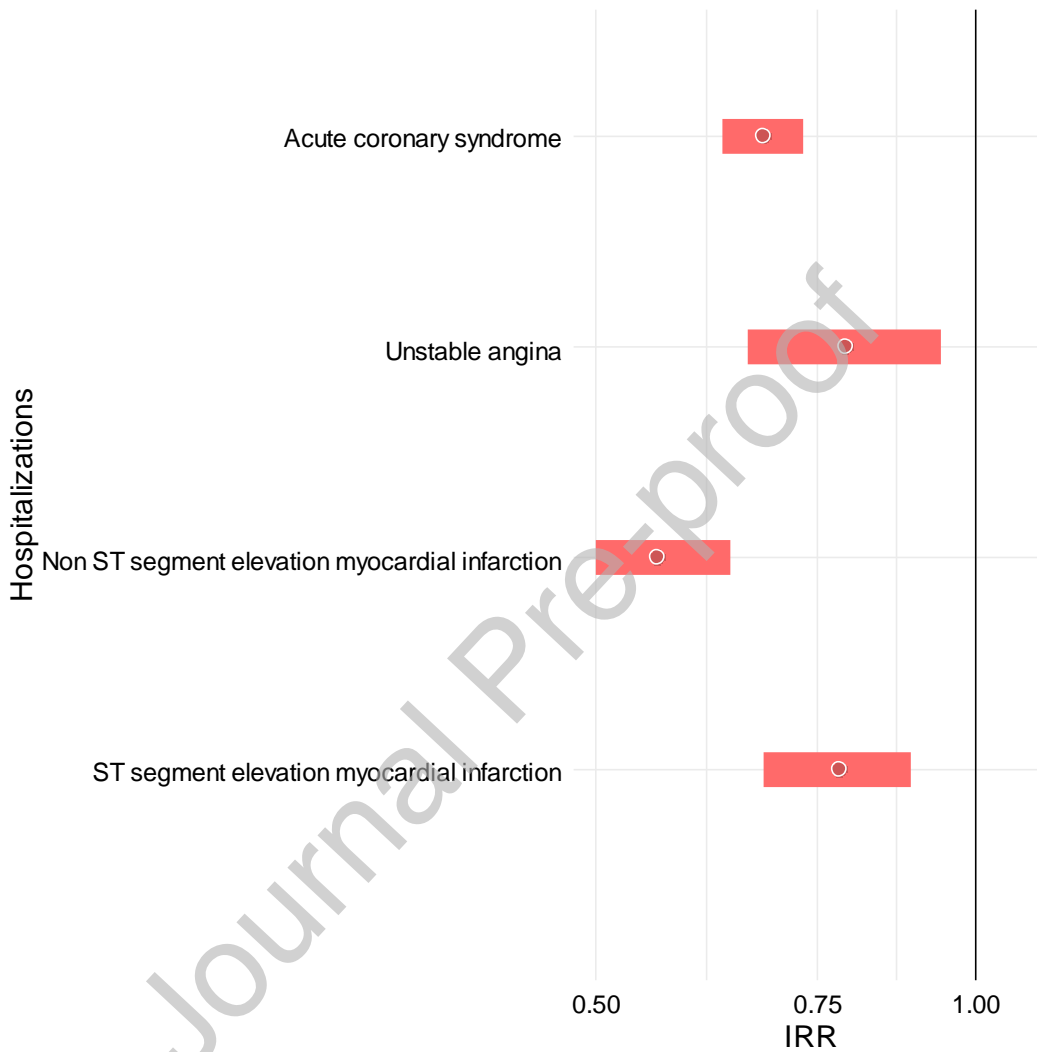
**FIGURE LEGENDS:**

Figure 1: Forest plots showing the incidence-rate ratios (IRR) of the primary causes of hospitalisation between the study period (2020) and the control period (2019).



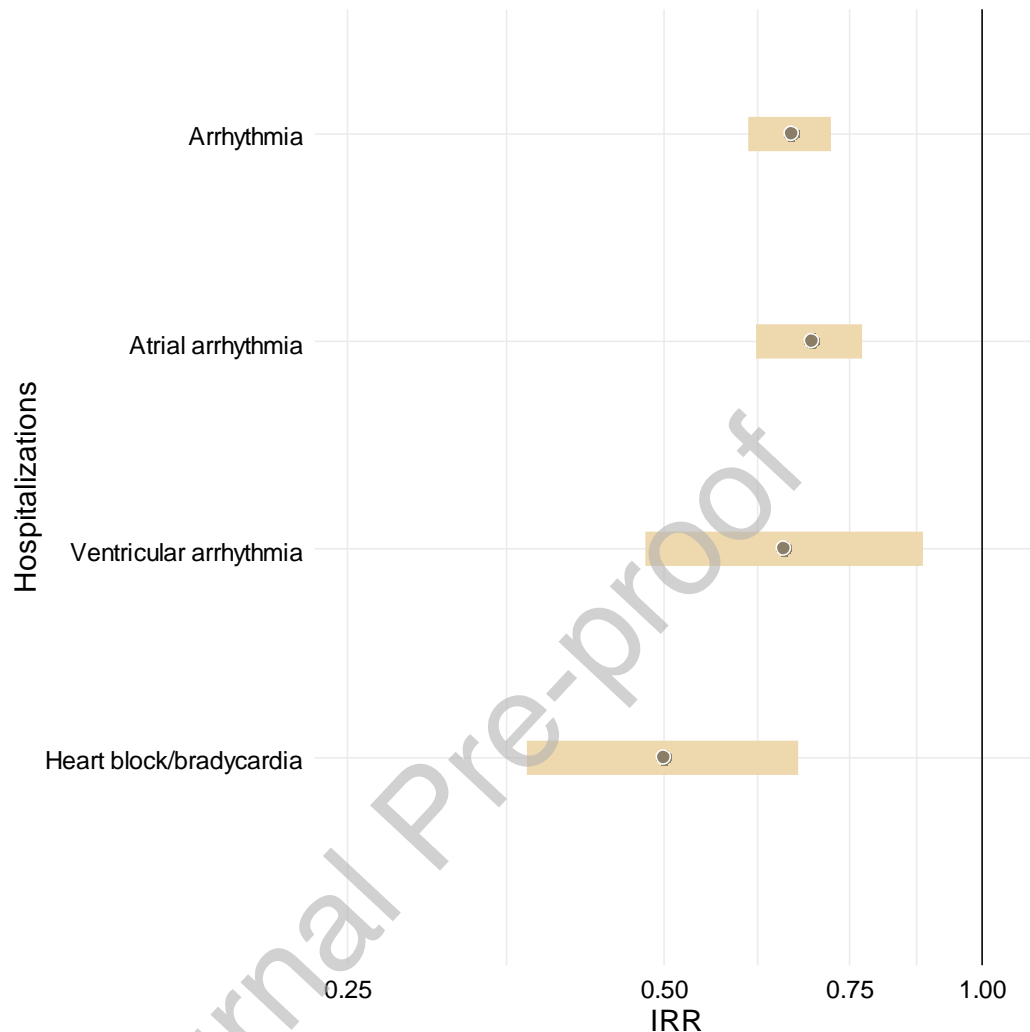
**Figure 1** Forest plots showing the incidence-rate ratios of the primary causes of hospitalisation between the study period (2020) and the control period (2019).

Figure 2: Forest plots showing the incidence-rate ratios (IRR) of acute coronary syndrome categories between the study period (2020) and the control period (2019).



**Figure 2** Forest plots showing the incidence-rate ratios of acute coronary syndrome categories between the study period (2020) and the control period (2019).

Figure 3: Forest plots showing the incidence-rate ratios of arrhythmia categories between the study period (2020) and the control period (2019).



**Figure 3** Forest plots showing the incidence-rate ratios of arrhythmia categories between the study period (2020) and the control period (2019).

**TABLE LEGENDS:**

**Table 1.** Comparison of patients numbers and primary cause of admission at cardiology departments between the study period (2020) and the control period (2019).

**Table 2.** Comparison of patient profiles at cardiology departments between the study period (2020) and the control period (2019).

**Table 3.** Comparison of acute coronary syndrome categories between the study period (2020) and the control period (2019).

**Table 4.** Comparison of arrhythmias categories between the study period (2020) and the control period (2019).

Table 1. Comparison of patients numbers and primary cause of admission at cardiology departments between the study period (2020) and the control period (2019).

	<b>All, n</b>	<b>Study period Year 2020</b>	<b>Control period Year 2019</b>
<b><u>Acute coronary syndrome, n</u></b>	<b>2803</b>	<b>1132</b>	<b>1671</b>
IRR (95% CI)		0.68 (0.63-0.73)	
<b><u>Acute heart failure, n</u></b>	<b>1137</b>	<b>450</b>	<b>687</b>
IRR (95% CI)		0.65 (0.58-0.74)	
<b><u>Arrhythmia, n</u></b>	<b>1992</b>	<b>790</b>	<b>1202</b>
IRR (95% CI)		0.66 (0.60-0.72)	
<b><u>Pulmonary embolism, n</u></b>	<b>142</b>	71	71
IRR (95% CI)		1.00 (0.72-1.39)	
<b><u>Other, n</u></b>	<b>1379</b>	<b>564</b>	<b>821</b>
IRR (95% CI)		0.68 (0.62-0.76)	
IRR, incident rate ratio; 95%CI, 95% confidence interval;			

Table 2. Comparison of patient profiles at cardiology departments between the study period (2020) and the control period (2019).

	All	Study period Year 2020	Control period Year 2019	OR (95%CI)	p
<b>DEMOGRAPHY</b>					
<b>Gender, male, n (%)</b>	4774 (64)	1928 (64)	2846 (64)	1.01 (0.97- 1.04)	0.63
<b>Age ≥65 years, n (%)</b>	4714 (63)	<b>1842 (61)</b>	<b>2871 (64)</b>	<b>0.87 (0.79- 0.96)</b>	<b>&lt;0.01</b>
<b>CAUSE OF ADMISSION</b>					
<b>Acute coronary syndrome, n (%)</b>	2803 (37)	1132 (38)	1671 (38)	1.00 (0.95- 1.05)	0.88
<b>Acute heart failure, n (%)</b>	1137 (15)	450 (15)	687 (15)	0.96 (0.86- 1.08)	0.52
<b>Arrhythmia, n (%)</b>	1992 (27)	790 (26)	1202 (27)	0.96 (0.87- 1.07)	0.47
<b>Pulmonary embolism, n (%)</b>	<b>142 (1.9)</b>	<b>71 (2.3)</b>	<b>71 (1.6)</b>	<b>1.49 (1.07- 2.08)</b>	<b>0.02</b>
<b>Other, n (%)</b>	1379 (19)	564 (19)	821 (18)	1.02 (0.90- 1.15)	0.74
IRR, incident rate ratio; 95%CI, 95% confidence interval					

Table 3. Comparison of acute coronary syndrome categories between the study period (2020) and the control period (2019).

	<b>All, n (%)</b>	<b>Study period Year 2020</b>	<b>Control period Year 2019</b>	<b>OR (95%CI)</b>	<b>p</b>
<b>Acute coronary syndrome</b>					
<b>Unstable angina, n (%)</b> IRR (95%CI)	479 (19)	211 (21)	268 (18)	1.21 (0.99- 1.48)	0.06
		<b>0.79 (0.66-0.94)</b>			
<b>NSTEMI, n (%)</b> IRR (95%CI)	1126 (46)	<b>406 (41)</b>	<b>720 (49)</b>	<b>0.72 (0.61- 0.85)</b>	<b>&lt;0.0001</b>
		<b>0.56 (0.50-0.64)</b>			
<b>STEMI, n (%)</b> IRR (95%CI)	841 (34)	<b>368 (37)</b>	<b>473 (32)</b>	<b>1.24 (1.05- 1.48)</b>	<b>0.01</b>
		<b>0.78 (0.68-0.89)</b>			
IRR, incident rate ratio; 95%CI, 95% confidence interval; NSTEMI, non ST segment elevation myocardial infarction; STEMI, ST elevation myocardial infarction					



Table 4. Comparison of arrhythmias categories between the study period (2020) and the control period (2019).

	<b>All, n (%)</b>	<b>Study period Year 2020</b>	<b>Control period Year 2019</b>	<b>OR (95%CI)</b>	<b>p</b>
<b>Categories of arrhythmia</b>					
<b>Atrial arrhythmia, n (%)</b>	1193 (76)	487 (78)	706 (74)	1.21 (0.96-1.54)	0.11
<b>IRR (95%CI)</b>		<b>0.69 (0.6-0.77)</b>			
<b>Ventricular arrhythmia, n (%)</b>	177 (11)	70 (11)	107 (11)	0.99 (0.76-1.30)	0.96
<b>IRR (95%CI)</b>		<b>0.65 (0.48-0.88)</b>			
<b>Bradycardia, AV blocks, n (%)</b>	204 (13)	68 (11)	136 (14)	<b>0.73 (0.53-1.00)</b>	<b>&lt;0.05</b>
<b>IRR (95%CI)</b>		<b>0.50 (0.37-0.67)</b>			
IRR, incident rate ratio; 95%CI, 95% confidence interval; AV, atrioventricular					