A Retrospective Study Assessing the Effect of Infections in Myocardial Infarction Patients: Mortality and Complications

Antoine El Khoury (✉ akhoury8@gmail.com)

University of Balamand

Pascale Salameh

Institut National de Santé Publique, Épidémiologie Clinique et Toxicologie

Sarah Hammoudeh

University of Balamand

Ahmad El Mahmoud

University of Balamand

Tonia Harb

University of Balamand

Nadia Chamoun

University of Balamand

Aline Kalaydjian

University of Balamand

Lea Chalhoub

University of Balamand

Paul El Meouchy

University of Balamand

Sara Chendeb

University of Balamand

Samer Nasr

University of Balamand

Research Article

Keywords: myocardial infarction, infection, complications, mortality, wound infection, sputum infection, blood infection, urine infection

Posted Date: January 7th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1182873/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background: There is a well-established relationship between myocardial infarction and infection. Multiple articles describe the increased risk of myocardial infarction, both type 1 and 2, following an infectious process. However few articles have described the relation between concomitant myocardial infarction and infections on same admission mortality and complications.

Methods: The aim is to assess the effect of an acquired or concomitant infection on complications and mortality during hospitalized cases of myocardial infarction. 1197 patients of different types of myocardial infarction were studied in correlation to infectious processes. Cultures from different sites were collected and isolation of various bacterial agents were studied. Mortality and various complications were compared between infected and non-infected subjects. Pearson's chi squared test was used to compare percentages (or the Fisher exact test when expected values were lower than 5). Moreover, means were compared through ANOVA, after checking data normality and homoscedasticity. A likelihood ratio backward stepwise method was used to conduct dichotomous logistic regressions, taking dichotomous outcomes as dependent variables, and sociodemographic and biological characteristics as independent variables (potential confounders).

Results: Wound, sputum, blood and urine infections were associated with increased same admission mortality and complications. Microorganisms were then studied alone regardless of the site of infection and it was shown that *Escherichia Coli*, *Escherichia Coli* ESBL, *Candida Albicans*, *Pseudomonas Aeruginosa* and *Staphylococcus* of any type were significantly associated with same admission complications when associated with myocardial infarction. Length of stay was significantly elevated in patients with concomitant infection and it increased with the addition of positive cultures from different sites.

Conclusion: Concomitant infections with myocardial infarction significantly increase the risk of same admission complications, mortality and length of stay regardless of the site of infection and type of microorganisms.

Background

Myocardial infarction occurs when there is abrupt discontinuation of blood flow to the myocardial cells due to a coronary artery plaque [1]. Patients tend to present with acute onset typical chest pain in most cases [2]. Patients will require hospital admission and urgent coronary revascularization in the case of ST elevation myocardial infarction [3]. The prevalence of the disease increases with age and is associated with traditional risk factors such as hypertension and diabetes [4]. Patients with this condition should receive antiplatelets medications in addition to lipid lowering drugs [5]. When not adequately treated, patients are at risk of developing complications and the most common being cardiogenic shock following a reduction in systolic function resulting in elevation of intracardiac pressures leading to acute heart failure [6]. The mortality rate during the same admission is increased due to the development of complications such as heart failure and arrhythmias [7]. Non cardiac conditions contribute to the same admission mortality in patients presenting with myocardial infarction [8]. Infections contribute to morbidity and complications [9]. This is potentially caused by the release of cytokines and inflammatory mediators that exacerbate the condition [10]. Several articles

and reviews discuss post-infectious myocardial infarctions. However, studies must be conducted to assess the effect of infections on the course of disease in myocardial infarction patients.

Objective

The objective of this study is to compare mortality and complication rates in myocardial infarction (MI) patients with and without concurrent infections. We hypothesized infections in association with myocardial infarction contribute to higher mortality rates as compared to myocardial infarction alone regardless if the infections is associated with symptoms or is asymptomatic. We also aimed to study each microorganism regardless of the infection site and try to link the causative infectious agent with the pattern of increased mortality and complications.

Methods

Study Design:

This work is a retrospective study. Data was collected from hospitalized patients from 2009 to 2020 in a single center, Mount Lebanon Hospital University Medical Center. Patients were randomly selected based on the final diagnosis on the discharge paper.

Participants:

Patients included were diagnosed of having acute myocardial infarction of any type.

Myocardial infarction was defined as ST elevation myocardial infarction, non-ST elevation myocardial infarction and unstable angina.

Data Measurement:

Basic information was collected about patient's characteristics, duration of stay in the hospital, admission unit. Patients were also evaluated based on the presenting symptoms and signs. Data concerning the given treatment was also collected including medical therapy or emergent cardiac catheterization interventions. Data on mortality and complications was noted in addition to basic laboratory tests such as troponin, CRP, creatinine and platelets level. Different types of cultures were recorded, and data from wound, sputum, blood, and urine culture were collected in order to find a correlation with mortality and complications. The duration of hospital stay was evaluated in regard of positive cultures and presence or absence of a specific microorganism.

This trial was approved by Institutional Review Board IRB from the hospital research center.

Statistical Methods:

Data was analyzed using SPSS software, version 25.0. A descriptive part helped to summarize multiple data variables. Minimal and maximal values were collected with mean and standard deviations analysis. Pearson's chi squared test was used to compare percentages (or the Fisher exact test when expected values were lower than 5). Moreover, means were compared through ANOVA, after checking data normality and

homoscedasticity. A likelihood ratio backward stepwise method was used to conduct dichotomous logistic regressions, taking dichotomous outcomes as dependent variables, and sociodemographic and biological characteristics as independent variables (potential confounders). Adjusted OR were calculated, along with their 95% confidence interval.

Results

Our study included 1197 subjects, out of which 844 (70.5%) were males and 353 (29.5%) were females, with an average age of 67.9 years ($\pm$ 13.1). The youngest patient diagnosed with myocardial infarction was a 22-year-old male. The average hospital stay was 7.5 days ($\pm$ 8.9 days) (Table 1). In addition, 397 (33.17%) of the patients were admitted to the ICU, 571 (47.70%) were admitted to CCU and 217 (18.13%) were admitted to regular floor. Data was missing for 12 patients (1.00%) (Table 2). Overall, in-hospital mortality during same admission was 13.03% (155/1197 patients).

The baseline characteristics of patients concerning age, duration of stay, admission systolic blood pressure, diastolic blood pressure, temperature, troponin level and CRP level are summarized in Table 1. Social history of patients was evaluated and 56.47% of patients were active smokers, 16.21% were excessive caffeine consumers and 7.69% were active alcoholics (Table 2).

Table 1
Patients characteristics regarding age, duration of hospital stay and some admission laboratory values.

Baseline Characteristics	Minimum	Maximum	Mean	Std. Deviation
Age (years)	23	102	67.94	13.13
Duration of stay (days)	0	146	7.54	8.98
BMI (kg/m ²)	15.43	47.35	27.27	4.86
SBP (mmHg)	38	230	126.32	26.37
DBP (mmHg)	20	130	71.65	14.86
Temperature (°C)	34	42.2	36.91	0.66
Troponin (ng/ml)	0	91	5.33	11.69
CRP (mg/L)	1	528	57.31	81.04

Table 2
Patients characteristics on admission regarding gender, social habits, and admission unit (frequency and percentages).

Gender	Number N	Percentage %
Male	844	70.51%
Female	353	29.49%
Social Habits	Number N	Percentage %
Tabaco	676	56.47%
Caffeine	194	16.21%
Alcohol	92	7.69%
Admission Unit	Number N	Percentage %
ICU	397	33.17%
CCU	571	47.70%
Regular Floor	217	18.13%
<i>Data Not Available</i>	<i>12</i>	<i>1.00%</i>

Patients with acute coronary syndrome (ST elevation myocardial infarction, non-ST elevation myocardial infarction and unstable angina) were evaluated based on the presence or absence of simultaneous infection. Patients were evaluated for wound infections, sputum infections, urinary tract infections and blood stream infections.

Wound Culture

Concomitant wound culture infections were observed in 49 patients presenting with MI. 14 out of 35 patients died as a result. The most common isolated germ in this category of patients was *Escherichia coli* observed in a total of 10 patients followed by *staphylococcus aureus* observed in 7 patients and *pseudomonas aeruginosa* in observed 6 patients. The rest of the bacteria and fungus can be observed in *table 3* (The number of infections is higher than 49 because few patients were infected by multiple germs at once).

Same admission mortality of any cause in patients with myocardial infarction and concomitant wound culture infection was evaluated. From the total 155 patients that died during the same admission, 14 patients had concomitant wound infection. There was a significant correlation and the p value was 0.001 making this correlation significant (Table 4.a).

All causes complications were also studied in comparison to concomitant wound culture infection. From the 49 patients that developed wound infection, 27 had same admission complications. The association was significant with a p value of 0.002 (Table 4.a).

Furthermore, when comparing different types of myocardial infarction with various sites of concomitant infections, we found that wound infections were mostly associated with NSTEMI and unstable angina compared to STEMI, with a significant p value of 0.034 (Table 4.b).

Table 4

a: Comparison of numbers and percentages of cases with and without complications and mortality between different sites of concomitant infections with positive cultures and their respective p values.

Sites of Concomitant Infection	Number of Cases	Without Complications	With Complications	P Value	Without Mortality	With Mortality	P Value
<i>Wound Culture</i>	49	22(44.9%)	27(55.1%)	0.002	35(71.4%)	14(28.6%)	0.001
<i>Sputum Culture</i>	107	40 (37.3%)	67(62.6%)	0.001	66(61.7%)	41(38.3%)	0.001
<i>Blood Culture</i>	47	17(36.2%)	30(63.8%)	0.001	29(61.7%)	18(38.3%)	0.001
<i>Urine Culture</i>	121	54(44.6%)	67(55.4%)	0.001	91(75.2%)	30(24%)	0.001

Table 4

b: Comparison of different myocardial infarction types between different sites of concomitant infections with positive cultures.

Sites of Concomitant Infection	STEMI	NSTEMI	Unstable Angina	Any Type MI	P Value
<i>Wound Culture</i>	1.2%	4.8%	4.26%	4.1%	0.034
<i>Sputum Culture</i>	8.4%	9.2%	6.38%	8.93%	0.758
<i>Blood Culture</i>	2.4%	4.44%	2.12%	3.92%	0.274
<i>Urine Culture</i>	7.6%	10.88%	8.51%	10.1%	0.291

Sputum Culture

Concomitant sputum culture infection was observed in 107 patients presenting with MI. 41 patients with sputum infection died as a result. 17 microorganisms were isolated from the sputum samples and the most common microorganism was a fungus, candida albicans in 39 patients followed by streptococcus viridans in 30 patients and Neisseria in 26 patients. The rest of organisms can be observed in table 3. (The number of infections is higher than 107 because few patients were infected by multiple germs at once).

Same admission mortality of any cause in patients with myocardial infarction and concomitant sputum culture infection was evaluated. From the total 155 patients that died during the same admission, 41 patients had concomitant sputum infection. There was a significant correlation and the p value was 0.001 making this correlation very significant (Table 4.a).

All causes complications were also studied in comparison to concomitant sputum culture infections. From the 107 patients that developed sputum infection, 67 had same admission complications. The association was significant with a p value of 0.001 (Table 4.a).

Blood culture

Concomitant blood culture infection was observed in 47 patients of patients with MI. 18 Patients with blood infection died as a result. 12 microorganisms were isolated from the blood samples and the most common microorganism was a bacterium, Escherichia coli in 17 patients followed by Staphylococcus coagulase negative in 16 and E.coli ESBL in 9. The rest of organisms can be observed in table 3 (The number of infections is higher than 107 because few patients were infected by multiple germs at once).

Same admission mortality of any cause in patients with myocardial infarction and concomitant blood culture infection was evaluated. From the total 155 patients that died during the same admission, 18 patients had concomitant blood infection. There was a significant correlation and the p value was 0.001 making this correlation very significant (Table 4.a).

All causes complications were also studied in comparison to concomitant blood culture infections. From the 47 patients that developed blood infection, 30 had same admission complications. The association was significant with a p value of 0.001 (Table 4.a).

Urine culture

Concomitant urine culture infection was observed in 121 patients of patients with MI. 30 Patients with urine infection died as a result. 16 microorganisms were isolated from the urine samples and the most common microorganism was the bacterium E.coli in 67 patients followed by E.coli ESBL in 27 patients and Candida Albicans in 26. The rest of organisms can be observed in table 3 (The number of infections is higher than 121 because few patients were infected by multiple germs at once).

Same admission mortality of any cause in patients with myocardial infarction and concomitant urine culture infection was evaluated. From the total 155 patients that died during the same admission, 30 patients had concomitant urine infection. There was a significant correlation and the p value was 0.001 making this correlation very significant (Table 4.a).

All causes complications were also studied in comparison to concomitant urine culture infections. From the 121 patients that developed urine infection, 67 had same admission complications. The association was significant with a p value of 0.001 (Table 4.a).

The most common cause of death was cardiogenic shock in 124 cases followed by septic shock in 34 cases. Ventricular arrhythmias occurred in 6 patients while pericardial tamponade and complete AV block occurred in 2 and 1 patients respectively. Most patients had combination of causes, especially patients with concomitant infections with high risk of septic shock complicating cardiogenic shock and leading to higher mortality rates.

Microorganisms were then subdivided by type of bacteria, virus, or fungi and regardless of site of infection. The presence of a specific microorganism was first studied in relation to myocardial infarction type and the percentages of each microorganism was calculated in all groups of myocardial infarctions. E. coli was the most prevalent bacteria in patients with NSTEMI and unstable angina ($p=0.041$) while Candida albicans was most prevalent in case of STEMI (Table 5.a). The same microorganisms were studied in relation to all causes mortality and all causes complications during the same admission (Table 5.b). The presence of Pseudomonas, Escherichia coli ESBL, Candida albicans, Escherichia coli staphylococcus and streptococcus at any site were associated with same admission complications of any type and the correlation was significant.

A significant correlation was established between death and the presence of pseudomonas, Escherichia coli ESBL, Candida albicans, klebsiella pneumonia, E. coli, Enterobacter, Acinetobacter, and Staphylococcus at any site (Table 5.b).

Table 5

a: Distribution of different myocardial infarction types among different microorganisms isolated from positive culture sites.

Microorganisms at any Site	STEMI	NSTEMI	Unstable Angina	Any Type MI	P Value
<i>Pseudomonas</i>	2.8%	1.4%	0%	1.7%	0.221
<i>Escherichia Coli ESBL</i>	2.8%	3.2%	2.1%	3.1%	0.875
<i>Candida albicans</i>	5.6%	5.2%	5.1%	5.1%	0.261
<i>Klebsiella pneumonia</i>	2.4%	1.3%	0%	1.5%	0.325
<i>E. coli</i>	4%	8.8%	8.5%	7.8%	0.043
<i>Enterococcus</i>	0%	0.6%	0%	0.4%	0.437
<i>Enterobacter</i>	0%	1%	0%	0.8%	0.224
<i>Acinetobacter</i>	0.8%	1.1%	0%	1%	0.71
<i>Staphylococcus</i>	1.2%	3.9%	4.3%	3.3%	0.15%

Table 5

b: Distribution of cases with and without complications and mortality among positive cultures of different microorganisms causing concomitant infections and their respective p values.

Microorganisms at any Site	Number of Cases	Cases Without Complications	Cases With Complications	P Value	Cases Without Mortality	Cases With Mortality	P Value
<i>Pseudomonas</i>	20	7 (35%)	13 (65%)	0.003	13 (65%)	7 (35%)	0.003
<i>Escherichia Coli ESBL</i>	37	14 (37.8%)	23 (62.2%)	0.001	21 (56.8%)	16 (43.2%)	0.001
<i>Candida albicans</i>	61	21 (34.4%)	40 (65.6%)	0.001	36 (59%)	25 (41%)	0.001
<i>Klebsiella pneumonia</i>	18	9 (50%)	9 (50%)	0.154	12 (66.7%)	6 (33.3%)	0.009
<i>E. coli</i>	93	39 (41.9%)	54 (58.1%)	0.001	69 (74.2%)	24 (25.8%)	0.001
<i>Enterococcus</i>	5	2 (40%)	3 (60%)	0.222	3 (60%)	2 (40%)	0.071
<i>Enterobacter</i>	9	5 (55.6%)	4 (44.4%)	0.514	5 (55.6%)	4 (44.4%)	0.005
<i>Acinetobacter</i>	12	6 (50%)	6 (50%)	0.254	8 (66.7%)	4 (33.3%)	0.035
<i>Staphylococcus</i>	40	13 (32.5%)	27 (67.5%)	0.001	27 (67.5%)	13 (32.5%)	0.001
<i>Streptococcus</i>	37	18 (48.6%)	19 (51.4%)	0.025	29 (78.4%)	8 (21.6%)	0.11

The effect of infections on hospital stay was studied and it was found that patients with myocardial infarction of any type had an average of 7.5 days (SD = 8.9 days) before outcome (discharge home or death) (Table 1). When excluding patients that developed infections during the same admission, the average hospital stay for patients with myocardial infarction without evidence of infections dropped to 6.0 days (SD = 5.9 days). Patients were then evaluated based on the presence of a positive culture and were divided in three groups. The group with a single site positive culture (Wound, sputum, blood or urine) had a 12.1 days average (SD = 13.5 days) stay in the hospital, double the number of days of patients without infections. The addition of a second positive culture in a different site in patients with MI significantly increased the average length of stay to 16.7 days (SD = 17.2 days). The addition of a third positive culture in the group of MI with three sites of positive cultures had a modest increase in length of stay to reach 17.3 days (SD = 17.9 days) on average. The results are shown and summarized in the stacked line graph 1.

Graph 1: Graph showing the increase in number of days spent in hospital in myocardial infarction patient without any infection, with infection at one, two and three different sites.

When dividing patients according to the site of positive culture, it was shown that patients with a positive blood culture had the longest hospital stay reaching 17.2 days (SD = 15.8 Days) in average followed by

sputum culture group averaging 15.3 days (SD = 18.9 Days). Patients with positive wound or urine cultures had similar results with 12 (SD = 8.7 Days) days and 11.7 days (SD = 12.2 Days) respectively. The results are shown and summarized in the clustered bar graph 2.

Graph 2: Length of hospital stay in days for patients with Myocardial infarction (MI) without infection, with wound, sputum, blood, and urine infection.

When comparing each microorganism individually, regardless of the site of culture, the presence or absence of a specific microorganism was evaluated. Patients with *Acinetobacter baumannii* infection at any site had the longest hospital stay of 25 days (SD = 22.8 Days) in average followed by patients with *E.coli* ESBL with 18.45 days (SD = 26.9 Days) and *Klebsiella pneumonia* with 17.1 days (SD = 20.6 Days) as can be seen in clustered bar graph 3. The full results of the hospital stay when compared to all subgroups of patients is summarized in a descriptive analysis Table 6a, Table 6.b and Table 6.c.

Table 6
a: Comparison of number of days spent in hospital in patients with different microorganisms isolated from positive culture sites.

Days of Hospital Stay				
Type of Microorganism at any Site	Minimum	Maximum	Mean	Std. Deviation
<i>Pseudomonas</i>	3	18	7.83	4.28
<i>Escherichia Coli ESBL</i>	2	146	18.45	26.85
<i>Candida albicans</i>	1	75	13.47	11.7
<i>Klebsiella pneumonia</i>	1	75	17.05	20.6
<i>E. coli</i>	1	133	13.22	17.87
<i>Enterococcus</i>	3	28	12.75	10.71
<i>Enterobacter</i>	3	21	10.85	7.49
<i>Acinetobacter</i>	7	85	25	22.76
<i>Staphylococcus</i>	1	85	14.67	14.75
<i>Streptococcus</i>	2	55	12.41	11.02

Table 6

b: Comparison of number of days spent in hospital in patients with different sites of positive cultures.

Days of Hospital Stay				
Site of Concomitant infection	Minimum	Maximum	Mean	Std. Deviation
<i>Wound Infection</i>	1	37	12	8.66
<i>Sputum Infection</i>	1	146	15.25	18.91
<i>Blood Infection</i>	2	85	17.2	15.84
<i>Urine Infection</i>	1	75	11.72	12.18

Table 6

c: Comparison of number of days spent in hospital in patients with different number of positive culture sites.

Days of Hospital Stay				
Number of positive culture Sites	Minimum	Maximum	Mean	Std. Deviation
MI + Zero Sites	0	67	6.02	5.91
MI + One Sites	1	146	12.09	13.51
MI + Two Sites	1	85	16.73	17.26
MI + Three Sites	3	55	17.28	17.97

Multivariable analysis

When studying the relation between mortality in patients with infection with other factors (Table 7a), it was shown that all these factors were significantly associated with increased mortality, except for high and very high blood pressure (high blood pressure was considered in our study as a systolic blood pressure between 140 mmHg and 160 mmHg and very high blood pressure as systolic blood pressure above 170 mmHg). Also, alcohol consumption gave a borderline result. Complications post MI were significantly associated with the factors reported in the model, except for an inverse association with High and very high blood pressure, high uric acid (all levels above 7 were considered as a high uric acid in our study), and chest pain, that were associated with lower risk of complications (Table 7b).

Table 7

a: Mortality, with infection factors detailed (To note that the number range that we used in our study is detailed in the first column of the table)

Factor	Beta	P-value	ORa	Lower bound of ORa	Upper bound of ORa
Age in years	.066	.000	1.068	1.043	1.093
BMI Overweight >25	.934	.011	2.545	1.233	5.251
BMI Underweight <18.5	3.797	.000	44.566	9.011	220.421
Systolic BP High (140 to 170mm Hg)	-.986	.018	.373	.165	.844
Systolic BP Very High (>170 mmHg)	-1.033	.033	.356	.138	.921
Systolic BP Very low (<80 mmHg)	1.430	.014	4.179	1.342	13.016
Heart rate Very High (>130 BPM)	2.538	.074	12.656	.782	204.848
Platelets level Extremely low (0 to 49 000)	2.082	.024	8.022	1.310	49.121
Platelets level Very low (50000 to 99000)	1.690	.000	5.418	2.330	12.596
Calcium level Extremely low (0.1 to 6.0)	2.228	.043	9.280	1.078	79.912
Calcium level Very low (6 to 7.5)	2.152	.000	8.599	3.555	20.796
CVA	1.220	.017	3.386	1.242	9.228
atrial fibrillation	1.218	.010	3.380	1.337	8.544
Asthma	2.993	.002	19.952	3.035	131.170
Alcohol	.314	.062	1.368	.984	1.902

Table 7

b: Any complication with infectious factors detailed (To note that the number range that we used in our study is detailed in the first column of the table)

Factor	Beta	P-value	ORa	Lower bound of ORa	Upper bound of ORa
Age in years	.075	.000	1.078	1.046	1.111
Systolic BP High (140 to 170 mmHg)	-1.383	.012	.251	.085	.740
Systolic BP Low (80 to 100 mmHg)	1.067	.014	2.906	1.241	6.802
Systolic BP Very High (>170 mmHg)	-1.220	.052	.295	.086	1.008
Platelets level Extremely low (0 to 49 000)	2.852	.008	17.315	2.085	143.772
Platelets level Very low (50000 to 99000)	1.736	.004	5.674	1.720	18.717
Uric acid level High (>7.0)	-2.582	.007	.076	.012	.493
Chest pain	-.789	.013	.454	.243	.849
Shoulder pain	2.457	.013	11.664	1.666	81.680
Seizure	4.463	.003	86.720	4.365	1723.064
CKD	1.052	.004	2.865	1.413	5.808
Lymphoma	3.067	.040	21.471	1.153	399.917
Hypothyroidism	1.909	.008	6.747	1.631	27.908
Hyperthyroidism	4.318	.009	75.058	2.956	1905.982
Anticoagulation	1.133	.004	3.106	1.423	6.779
Alcohol	1.283	.007	3.609	1.423	9.154

Discussion

Acute coronary occlusion will lead to myocardial infarction referred as type 1 MI [11]. Infections are postulated to be a trigger factor for the rapid development of atherosclerosis [12]. Autopsies done in animal models have shown that infections and systemic inflammations have caused increased atheromatous activities in coronary plaques [13]. Various cytokines and inflammatory mediators play a role such metalloproteinase and peptidases and they activate oxidative burst which will lead to unstable plaques [14].

Infections induce a hypercoagulable state promoting coronary thrombosis mainly in patients with underlying coronary atherosclerosis [15]. This mechanism is promoted by activation of neutrophils and platelets, in addition to activation of tissue factors, impaired coagulation cascade and alteration of endothelium function [16]. It was proven that patients with influenza and pneumonia had increased in myocardial infarction rates

due to activation of the hypercoagulable mediators [17]. This state of inflammation and thrombosis persisted beyond the infection duration and the risk of myocardial infarction persisted for longer periods [18].

Type 2 myocardial infarction occurs in case of increase in oxygen demands [11]. Infections and sepsis will cause lower blood pressure and increase in heart rates which will shorten diastole [19]. Coronary perfusion occurs in diastole and in case of infection, the coronary perfusion will be lower [20]. In cases of pneumonia, lower oxygen levels will impact myocardial oxygenation and promote ischemia leading to type 2 myocardial infarction [21].

Autopsies in animal models showed that ischemia in infections may occur due to increased myocyte vacuolization leading to loss of myocytes rather than coronary artery stenosis increasing the risk of arrhythmias and heart failure [14].

Patients who had received vaccines for different infections were shown to have decrease in myocardial infarction risk due to decrease in the inflammatory mediators and hypercoagulable state [22].

From the 1197 patients included in this study, 324 cultures came back positive. The cultures were taken from wound, sputum, blood, and urine samples. The most common cultures with positive results were urine cultures followed by sputum cultures. Sputum cultures were most often positive in patients with Myocardial infarction and admitted to the intensive care unit and requiring mechanical ventilation leading to ventilated associated pneumonia. Blood cultures and wound cultures were less common. Positive wound cultures were more common in diabetic patients, with chronic wounds or bed sores.

Patients were started on appropriate antithrombotic therapy and 467 received antibiotics due to simultaneous infection even if absence of positive cultures. The mortality rate during the same admission was 13.0%, 156 patients had death outcome and the most common cause of death was cardiogenic shock in 125 patients followed by septic shock in 35 patients. Two patients died from complete heart block, two from ventricular arrhythmias, two from pericardial tamponade and the cause of death was unspecified in two cases. The causes of mortality were similar to mortality in isolated myocardial infarction without the presence of infections with cardiogenic shock being the established most common cause of death during the same admission.

Complications without leading to mortality during the same admission were also studied and the most common being acute kidney injury seen followed by cardiogenic shock, pneumonia, DIC, pulmonary edema, atrial fibrillation, ventricular arrhythmias, and other less common complications. All complications were grouped in the same category of all causes complications, and it was confirmed that positive infections and cultures in wound, blood, sputum and urine were associated with increased risk of complications during the same admission with a significant p value. Acute kidney injury was very common, because infections and sepsis predispose the patient to hypotension and systemic vasodilation causing decrease renal perfusion and activation of the renin angiotensin aldosterone system [23]. This condition predisposes to prerenal azotemia and if remained untreated will lead to intrinsic renal damage and acute tubular necrosis leading to acute renal failure and many patients were started on dialysis consequently [24]. Cardiogenic shock was also significantly associated with patients that developed simultaneous infection with myocardial infarction. As in the case of renal failure, systemic infections will lead to systemic vasodilation in cases of septic shock leading to compensatory tachycardia as a response to preserve cardiac output [25]. The myocardium will compensate

early in the course of the disease but due to the additional strain from coronary artery disease, the heart muscles will fail and lead to cardiogenic shock requiring vasopressors and inotropes [26]. Cardiogenic shock will lead to pulmonary edema and ventricular arrhythmias exacerbating the condition [27].

Several studies were published regarding complications and mortality in myocardial infarction with concomitant infections and revealed results relatively in line with ours. A recent large study including 10,880,856 AMI admissions among which 745,536 cases of concomitant respiratory infections done by Vallabhajosyula et al. (2021) concluded that respiratory infections significantly impact AMI admissions with higher rates of complications, mortality, and resource utilization [28].

Concomitant influenza respiratory infection increased risk mortality and multi-organ failure in MI patients as well, however it was associated with decreased rate of cardiac angiography and revascularization events which was not investigated in our study (Cardoso et al., 2020) [29].

Lower utilization of percutaneous coronary intervention and coronary angiography was observed also by Parenica et al. (2017) in their observational study on acute MI patients presenting with cardiogenic shock as well [30]. But in contrast to the earlier literature findings and the ones in our study, Parenica et al. (2017) found no significant difference in mortality between infected and non-infected acute MI patients admitted with cardiogenic shock [30]. In fact, Patlolla et al. (2021) in their recent published article observed lower in-hospital mortality rate in acute myocardial infarction and cardiogenic shock patient complicated by respiratory infection compared to those with no infections, as well as lower utilization of coronary angiography and PCI which was attributed to higher rates NSTEMI-CS and lower rates of STEMI-CS in admissions with respiratory infections compared to those without [31].

Worse prognosis was not only limited to respiratory infections in the literature. While in our study, blood positive culture was relatively less common compared to sputum cultures, in other observational study of serious infections following myocardial infection, most of the infections were found to be isolated from the blood and demonstrated worse clinical outcome and longer hospital stay, which indicate that worse outcome is related to the infections in general and not only isolated to respiratory ones [9].

The second objective was to subdivide the microorganism by type regardless of the site of infection and correlate these findings with mortality and complications during the same admission. The reason of this selection is to try to identify a common link between the same microorganism present at different site and to detect a correlation with mortality. Some microorganisms secrete substances or toxins that can diffuse to the systemic circulation regardless of the site of origin. These substances will have an impact on the cardiac function leading to the development of complications and death. From the microorganisms studied in Table 6, only Enterococcus, Enterobacter and Acinetobacter were not significantly associated with the development of complications during the same admission, although Acinetobacter infections were strongly linked with mortality mainly in patients on mechanical ventilations and in the intensive care unit. Only streptococcus and enterococcus were not significantly correlated with mortality during the same admission with a p value of more than 0.05. To the best of our knowledge, no previous studies were done to investigate the effect of specific organisms in myocardial infarction patient who developed infectious process during their hospital stay.

Hospital length of stay is an important factor regarding cost of hospitalization, complications, and mortality. It is well established that the longer hospital stay is associated with major complications regardless of the initial diagnosis and the aim is to reduce the length of stay to promote and improve the health care system. Patients with myocardial infarction but with no evidence of infections or positive cultures were compared to patients with positive cultures in a single site, two sites and three sites. To note that when studying the length of stay, 66 patients were eliminated due to the unavailability of number of days of the admission. A total of 885 patients had myocardial infarction without the evidence of positive cultures and the length of stay was estimated to be 6 days. When a positive culture in a single site was added, there was a dramatic increase in the average length of stay to reach 12.1 days (198 patients had myocardial infarction and only a single site positive culture). The numbers kept on increasing when we added a second site and third site positive cultures. 41 patients had myocardial infarction with two cultures positive from different sites and 7 patients had MI with three positive cultures from three different sites and the length of stay increased to 16.7 days in the two sites group and 17.3 days in the three sites group. This is a logical interpretation because infections are known to cause serious problems and complications. The main point was to prove that the increase in sites of infections is directly proportional to number of complications and mortality since the latter is linked to the length of stay in hospital.

Patients were then subdivided based on the site of positive cultures and each group was compared to the group of patients with myocardial infarction but without a concomitant infection. The length of stay was the longest in the patients with positive blood cultures (17.2 days) with a total of 43 patients developing positive blood cultures. Blood stream infections are the main reasons for septic shock and require long duration of intravenous antibiotics to eliminate the microorganism. Antibiotics can cause a variety of side effects including acute renal injury requiring aggressive medical therapies to reverse the condition. All these factors combined will lead to the longest hospital duration of stay in this subgroup. Patients with myocardial infarction admitted to the intensive care unit are at risk of acquiring sputum infections, mainly patients on ventilators. A total of 100 patients developed sputum infection, and the duration of stay for these patients were on average 15.3 days, which is more than double the duration spent by MI patients without any infections (6 days). These results were in line with those found in previous studies demonstrating that indeed MI admissions with concomitant respiratory infection presenting with influenza [29] or with cardiogenic shock [31] have longer hospital stay and higher cost compared to those with no respiratory infections. Duration of hospital stay for patient with concomitant respiratory infection was slightly lower than those with bloodstream infections but higher than those with wound infections (45 patients averaging 12.0 days) and urine infections (113 patients averaging 11.7 days). Wound infections and urine infections are less severe types of infections that require lower antibiotics therapy duration and are a less frequent cause of septic shock as compared to blood and sputum culture infections.

Three germs, common in the intensive care setting, when studied regardless the positive culture site, showed that *Acinetobacter baumannii* was associated with the longest hospital stay reaching 25 days (total number of patients with this infection and myocardial infarction is 10 and all patients were admitted to the intensive care unit). Such infection requires broad spectrum antibiotics and are often resistant to most antimicrobial agents, requiring sometimes switching between therapies and pharmacological stewardship to decrease the bacterial resistance. These measures are essential for patient safety and to decrease the length of stay.

When using multivariable analysis, the mortality in patients with myocardial infarction was affected by many factors. But it was shown that patients with high or very high blood pressures (>140 mmHg) had lower level of mortality. This is potentially due to the fact that patients with higher blood pressures in the onset of myocardial infarction are treated more aggressively. By lowering blood pressure, afterload is lowered and myocardial strain will improve thus leading to improve outcomes. Similarly complications were associated with multiple factors but it was shown that higher blood pressure was a protective variable, similar to high uric acids. Patients with chest pain were found to have lower complications than patient without pain. Silent myocardial infarctions are more serious because of the lack of signs. In these cases, diagnosis is delayed or missed and the appropriate treatment is not administered, thus the higher incidence of complications in this subgroup.

Conclusion

Myocardial infarction is a serious and life-threatening condition that is associated with high rates of mortality. Patients with this condition will always require hospital admissions and long stays. This condition can lead to serious complications such as arrhythmias and heart failure. When infections were simultaneously associated to myocardial infarction, it was proven that patients had increased in rates of same admission mortality and complications. The results were applicable for patients with wound, sputum, blood and urine cultures infections. Microorganisms were then studied alone regardless of the site of infection, and it was shown that *Escherichia Coli*, *Escherichia Coli* ESBL, *Candida Albicans*, *Pseudomonas Aeruginosa* and *Staphylococcus* of any type were significantly associated with same admission complications when associated with myocardial infarction. *Escherichia Coli*, *Escherichia Coli* ESBL, *Candida Albicans*, *Pseudomonas Aeruginosa* *Staphylococcus* of any type, *Klebsiella Pneumonia*, *Enterobacter*, and *Acinetobacter Baumanii* were associated with same admission mortality in patients with myocardial infarction.

Patients with myocardial infarction without evidence of associated infections had lower length of stays in hospitals as compared to patients with myocardial infarction associated with positive wound, sputum, blood and urine. The longest hospitals stays were found in patients with positive blood cultures. Patients with myocardial infarction had longer hospital stays when they had positive cultures at multiple sites and the longest stays were found in patients with three positive cultures at different sites. Patients infected by *Acinetobacter Baumanii* had the longest duration of stay followed by *Escherichia Coli* ESBL.

Infections when associated with myocardial infarction, significantly increase the same admission complication, mortality and length of stay. Patients with myocardial infarction should be closely followed with infection preventive measures in order to avoid the two diseases association.

Multivariable analysis showed that higher blood pressures, high uric acid and chest pain were associated with less mortality and complications in patients with concomitant infections

Limitations

This study included one small pool of patient from a single hospital. Larger population pools and further retrospective and prospective studies must be conducted to assure and confirm the results found in our study.

More research must aim to build a firm relationship between different microorganisms infections and there effect on the course myocardial infarction hospitalization.

Abbreviations

MI: Myocardial infarction

CRP: C-Reactive protein

ICU: Intensive Care Unit

CCU: Cardiac Care Unit

BMI: Body mass index

SBP: Systolic blood pressure

DBP: Diastolic blood pressure

ECOLI: Escherichia Coli

SD: Standard deviation

AMI: Acute myocardial infarction

STEMI: ST segment elevation myocardial infarction

NSTEMI: Non ST segment elevation myocardial infarction

Declarations

All methods were carried out in accordance with the Declaration of Helsinki.

Ethics approval and consent to participate:

The approval of all the study protocol was given by the institutional research ethics committee at Mount Lebanon Hospital named “Ethics’ Committee of Mount Lebanon Hospital” in October 5, 2020. The approval was given until the study ends. The Ethics Committee operates under the understanding of Good Clinical Practice (GCP) under the guidance of the Declaration of Helsinki. All participants signed an informed participation consent.

Patient informed consent: This retrospective study is based on recorded data owned by “Mount Lebanon Hospital” and approval to use the data was obtained by its Ethics committee “Ethics’ Committee of Mount Lebanon Hospital”.

Consent for publication

All authors have approved the manuscript and agree with submission to this Journal.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no conflicts of interest.

Funding

Not funding was provided

Authors' contributions

A.E-K. designed and conducted the research. P.S. performed the statistical analysis. A.E-K and S.H. participated in writing. A.E-M., T.H., N.C., A.K., L.C., S.C., P.M., participated in data collection. S.N. supervised the study.

Acknowledgements

The authors would like to thank the staff of the archive department for making the data collection process simple and organized.

References

1. Williams, M. C., Moss, A. J., Dweck, M., Adamson, P. D., Alam, S., Hunter, A., Shah, A., Pawade, T., Weir-McCall, J. R., Roditi, G., van Beek, E., Newby, D. E., & Nicol, E. D. (2019). Coronary Artery Plaque Characteristics Associated With Adverse Outcomes in the SCOT-HEART Study. *Journal of the American College of Cardiology*, 73(3), 291–301. <https://doi.org/10.1016/j.jacc.2018.10.066>
2. Arora, G., & Bittner, V. (2015). Chest pain characteristics and gender in the early diagnosis of acute myocardial infarction. *Current cardiology reports*, 17(2), 5. <https://doi.org/10.1007/s11886-014-0557-5>
3. Lemkes, J. S., Janssens, G. N., van der Hoeven, N. W., van de Ven, P. M., Marques, K., Nap, A., van Leeuwen, M., Appelman, Y., Knaapen, P., Verouden, N., Allaart, C. P., Brinckman, S. L., Saraber, C. E., Plomp, K. J., Timmer, J. R., Kedhi, E., Hermanides, R. S., Meuwissen, M., Schaap, J., van der Weerdt, A. P., ... van Royen, N. (2019). Timing of revascularization in patients with transient ST-segment elevation myocardial infarction: a randomized clinical trial. *European heart journal*, 40(3), 283–291. <https://doi.org/10.1093/eurheartj/ehy651>
4. Kiani, F., Hesabi, N., & Arbabisarjou, A. (2015). Assessment of Risk Factors in Patients With Myocardial Infarction. *Global journal of health science*, 8(1), 255–262. <https://doi.org/10.5539/gjhs.v8n1p255>
5. Braunwald E. (2012). The treatment of acute myocardial infarction: the Past, the Present, and the Future. *European heart journal. Acute cardiovascular care*, 1(1), 9–12. <https://doi.org/10.1177/2048872612438026>

6. Ng, R., & Yeghiazarians, Y. (2013). Post myocardial infarction cardiogenic shock: a review of current therapies. *Journal of intensive care medicine*, 28(3), 151–165.
<https://doi.org/10.1177/0885066611411407>
7. Bhar-Amato, J., Davies, W., & Agarwal, S. (2017). Ventricular Arrhythmia after Acute Myocardial Infarction: 'The Perfect Storm'. *Arrhythmia & electrophysiology review*, 6(3), 134–139.
<https://doi.org/10.15420/aer.2017.24.1>
8. Saleh, M., & Ambrose, J. A. (2018). Understanding myocardial infarction. *F1000Research*, 7, F1000 Faculty Rev-1378. <https://doi.org/10.12688/f1000research.15096.1>
9. Truffa, A. A., Granger, C. B., White, K. R., Newby, L. K., Mehta, R. H., Hochman, J. S., Patel, M. R., Pieper, K. S., Al-Khalidi, H. R., Armstrong, P. W., & Lopes, R. D. (2012). Serious infection after acute myocardial infarction: incidence, clinical features, and outcomes. *JACC. Cardiovascular interventions*, 5(7), 769–776.
<https://doi.org/10.1016/j.jcin.2012.03.018>
10. Mann D. L. (2015). Innate immunity and the failing heart: the cytokine hypothesis revisited. *Circulation research*, 116(7), 1254–1268. <https://doi.org/10.1161/CIRCRESAHA.116.302317>
11. Gupta, S., Vaidya, S. R., Arora, S., Bahekar, A., & Devarapally, S. R. (2017). Type 2 versus type 1 myocardial infarction: a comparison of clinical characteristics and outcomes with a meta-analysis of observational studies. *Cardiovascular diagnosis and therapy*, 7(4), 348–358. <https://doi.org/10.21037/cdt.2017.03.21>
12. Sessa, R., Pietro, M. D., Filardo, S., & Turriziani, O. (2014). Infectious burden and atherosclerosis: A clinical issue. *World journal of clinical cases*, 2(7), 240–249. <https://doi.org/10.12998/wjcc.v2.i7.240>
13. Madjid, M., Vela, D., Khalili-Tabrizi, H., Casscells, S. W., & Litovsky, S. (2007). Systemic infections cause exaggerated local inflammation in atherosclerotic coronary arteries: clues to the triggering effect of acute infections on acute coronary syndromes. *Texas Heart Institute journal*, 34(1), 11–18.
14. Phatharajaree, W., Phrommintikul, A., & Chattipakorn, N. (2007). Matrix metalloproteinases and myocardial infarction. *The Canadian journal of cardiology*, 23(9), 727–733.
[https://doi.org/10.1016/s0828-282x\(07\)70818-8](https://doi.org/10.1016/s0828-282x(07)70818-8)
15. Beristain-Covarrubias, N., Perez-Toledo, M., Thomas, M. R., Henderson, I. R., Watson, S. P., & Cunningham, A. F. (2019). Understanding Infection-Induced Thrombosis: Lessons Learned From Animal Models. *Frontiers in immunology*, 10, 2569. <https://doi.org/10.3389/fimmu.2019.02569>
16. Kapoor, S., Opneja, A., & Nayak, L. (2018). The role of neutrophils in thrombosis. *Thrombosis research*, 170, 87–96. <https://doi.org/10.1016/j.thromres.2018.08.005>
17. Muscente, F., & De Caterina, R. (2020). Causal relationship between influenza infection and risk of acute myocardial infarction: pathophysiological hypothesis and clinical implications. *European heart journal supplements: journal of the European Society of Cardiology*, 22(Suppl E), E68–E72.
<https://doi.org/10.1093/eurheartj/suaa064>
18. Kulick, E. R., Alvord, T., Canning, M., Elkind, M., Chang, B. P., & Boehme, A. K. (2021). Risk of stroke and myocardial infarction after influenza-like illness in New York State. *BMC public health*, 21(1), 864.
<https://doi.org/10.1186/s12889-021-10916-4>
19. Fairchild, K. D., Srinivasan, V., Moorman, J. R., Gaykema, R. P., & Goehler, L. E. (2011). Pathogen-induced heart rate changes associated with cholinergic nervous system activation. *American journal of*

- physiology. Regulatory, integrative and comparative physiology*, 300(2), R330–R339.
<https://doi.org/10.1152/ajpregu.00487.2010>
20. Goodwill, A. G., Dick, G. M., Kiel, A. M., & Tune, J. D. (2017). Regulation of Coronary Blood Flow. *Comprehensive Physiology*, 7(2), 321–382. <https://doi.org/10.1002/cphy.c160016>
 21. Tralhão, A., & Póvoa, P. (2020). Cardiovascular Events After Community-Acquired Pneumonia: A Global Perspective with Systematic Review and Meta-Analysis of Observational Studies. *Journal of clinical medicine*, 9(2), 414. <https://doi.org/10.3390/jcm9020414>
 22. MacIntyre, C. R., Mahimbo, A., Moa, A. M., & Barnes, M. (2016). Influenza vaccine as a coronary intervention for prevention of myocardial infarction. *Heart (British Cardiac Society)*, 102(24), 1953–1956. <https://doi.org/10.1136/heartjnl-2016-309983>
 23. Muñoz-Durango, N., Fuentes, C. A., Castillo, A. E., González-Gómez, L. M., Vecchiola, A., Fardella, C. E., & Kalergis, A. M. (2016). Role of the Renin-Angiotensin-Aldosterone System beyond Blood Pressure Regulation: Molecular and Cellular Mechanisms Involved in End-Organ Damage during Arterial Hypertension. *International journal of molecular sciences*, 17(7), 797. <https://doi.org/10.3390/ijms17070797>
 24. Lehman, L. W., Saeed, M., Moody, G., & Mark, R. (2010). Hypotension as a Risk Factor for Acute Kidney Injury in ICU Patients. *Computing in cardiology*, 37, 1095–1098.
 25. Hotchkiss, R. S., Moldawer, L. L., Opal, S. M., Reinhart, K., Turnbull, I. R., & Vincent, J. L. (2016). Sepsis and septic shock. *Nature reviews. Disease primers*, 2, 16045. <https://doi.org/10.1038/nrdp.2016.45>
 26. Jardin, F., Brun-Ney, D., Auvert, B., Beauchet, A., & Bourdarias, J. P. (1990). Sepsis-related cardiogenic shock. *Critical care medicine*, 18(10), 1055–1060. <https://doi.org/10.1097/00003246-199010000-00001>
 27. Bhar-Amato, J., Davies, W., & Agarwal, S. (2017). Ventricular Arrhythmia after Acute Myocardial Infarction: 'The Perfect Storm'. *Arrhythmia & electrophysiology review*, 6(3), 134–139. <https://doi.org/10.15420/aer.2017.24.1>
 28. Vallabhajosyula, S., Patlolla, S. H., Murphree, D. H., Cheungpasitporn, W., Holme, D. R., Jr, & Gersh, B. J. (2021). Temporal Trends, Management and Outcomes of Acute Myocardial Infarction with Concomitant Respiratory Infections. *The American journal of cardiology*, 150, 1–7. <https://doi.org/10.1016/j.amjcard.2021.03.037>
 29. Cardoso, R., Rivera, M., Czarny, M. J., Knijnik, L., Fernandes, A., Blumenthal, R. S., Hasan, R. K., & Schulman, S. P. (2020). In-Hospital Management and Outcomes of Patients With Acute Myocardial Infarction and Influenza. *The American journal of cardiology*, 125(6), 840–844. <https://doi.org/10.1016/j.amjcard.2019.12.032>
 30. Parenica, J., Jarkovsky, J., Malaska, J., Mebazaa, A., Gottwaldova, J., Helanova, K., Litzman, J., Dastyh, M., Tomandl, J., Spinar, J., Dostalova, L., Lokaj, P., Tomandlova, M., Pavkova, M. G., Sevcik, P., Legrand, M., & GREAT Network (2017). Infectious Complications and Immune/Inflammatory Response in Cardiogenic Shock Patients: A Prospective Observational Study. *Shock (Augusta, Ga.)*, 47(2), 165–174. <https://doi.org/10.1097/SHK.0000000000000756>
 31. Patlolla, S. H., Sundaragiri, P. R., Cheungpasitporn, W., Doshi, R., & Vallabhajosyula, S. (2021). Impact of concomitant respiratory infections in the management and outcomes acute myocardial infarction-cardiogenic shock. *Indian heart journal*, 73(5), 565–571. <https://doi.org/10.1016/j.ihj.2021.07.004>

Tables

Due to technical limitations, table 3 is only available as a download in the Supplemental Files section.

Figures

Figure 1

Graph showing the increase in number of days spent in hospital in myocardial infarction patient without any infection, with infection at one, two and three different sites.

Figure 2

Length of hospital stay in days for patients with Myocardial infarction (MI) without infection, with wound, sputum, blood, and urine infection.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table03.png](#)