

DOI: 10.21767/1989-5216.1000205

Community Acquired Pneumonia (CAP), Type 2 Myocardial Infarction (Type 2 MI), and 5 Years Mortality after Discharge

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Abstract

Background: Epidemiologic studies demonstrated that community acquired pneumonia is associated with increased risk for cardiovascular events. Type 2 MI has been shown to predict a grave outcome, but the long term outcome of patients admitted with CAP who had also type 2 MI has not been studied.

Methods: during the years 2010-2016 all patients that were admitted with CAP were included in this retrospective study, and parameters like type 2 MI, age, gender, type 2 diabetes mellitus and renal failure were collected. The 5 years post discharge mortality rate was analyzed in relation with the clinical parameters.

Results: A total of 1751 consecutive patients were studied, 1222 died during the 5 years follow-up. Type 2 MI during hospitalization with CAP was associated with a higher mortality rate during the follow-up period (38.6% vs. 26.8%). Mortality rate was also dependent on older age and on renal failure.

Regression logistic analysis demonstrated an odds ratio of 19.90 to die after discharge for patients admitted with CAP who developed type 2 MI on admission or during hospitalization, and an odds ratio of 2.054 to die in CAP patients who suffered from renal failure.

Conclusions: Type 2 MI predicted a higher mortality rate during the 5 years follow up post discharge with odds ratio of 19.90. We recommend to modify the risk stratification of patients admitted with CAP and to consider type 2 MI as a risk factor for a long term outcome of patients admitted with CAP, especially older patients and those who suffer from renal failure.

Keywords: Renal failure; Cardiovascular events; Mortality rate

Background

Epidemiologic studies demonstrated that community acquired pneumonia (CAP) is associated with increased risk for cardiovascular events and acute myocardial infarction [1-6]. Increased concentrations of pro-inflammatory cytokines may trigger endothelial dysfunction and plaque rupture, and risk of development of myocardial infarction is greater for patients with infection associated with a strong inflammatory response [6]. Patients admitted with CAP have high levels of circulating pro-inflammatory cytokines [7]. Increased levels of cardiac troponins have been associated with more severe CAP [8,9]. A retrospective study that investigated the mortality rate among 220 patients with CAP found that patients who had increased levels of cardiac troponin I had a higher mortality rate [10].

We conducted a retrospective study that followed patients admitted with CAP for 5 years after hospitalization.

Our hypothesis was that patients admitted with CAP who also developed type 2 MI will have a higher mortality rate during the 5 years period after discharge from the hospital.

Methods

A retrospective study that followed 1751 patients admitted with CAP to our hospital, a regional community medical center in the north of Israel. The population was composed of Jews, Arabs, and Druze patients in equal numbers. The study was conducted during the years 2010-2016, and data was collected including age, gender, troponin levels without electrocardiographic (ECG) ST-T changes (type 2 MI), type 2 Diabetes Mellitus, chronic renal failure, and mortality up to 5 years after discharge from the hospitalization.

Definitions

Type 2 Myocardial Infarction (type 2 MI)-an increase of troponin I level without any ST-T change in the ECG or any change in wall motion detected by echocardiography.

Renal failure-creatinine level in blood more than 1.3 mg/ml.

Statistical analysis

Student's t-test and X² test were used to compare between patients admitted with CAP, who had troponin I (T) level higher than 0.028 ng/ml (without any ST-T changes in at least 2 recordings of the ECG) to those who were admitted with normal troponin levels (lower than 0.028 ng/ml).

In order to study the effect of type 2 MI on the long term mortality after discharge from the hospital, and to find the effects of age, gender, type 2 Diabetes Mellitus and renal failure on mortality rate after discharge, we used logistic regression analysis.

Results

1751 were recruited over 6 years (2010-2016), 942 women and 809 men (53.8% and 46.2%, p=NS), the age was 73.60 ± 14.21 years old (**Table 1**).

Table 1 Clinical characteristics.

Total	Men	Women	Age (y)	Type 2	MI	DM
1751	809	942	73.60 ± 14.21	500	165	152

Older patients had a higher rate of type 2 MI (mean age of patients with type 2 MI was 78.73 ± 11.17 years old, compared to patients without was 71.55 ± 14.76 years old, p<0.05 (T test). No gender effect was observed in relation to type 2 MI. There were 257 men (51.4%) and 243 women (48.6%) with type 2 MI (p=0.203, Pearson Chi Square test). No significant difference was observed between patients with type 2 MI and those without MI in relation to type 2 Diabetes Mellitus (type 2 DM). Among the 152 patients who had type 2 DM, only 34 had type 2 MI (6.8%) compared with 118 DM patients who did not (9.44%), p=0.07 (Pearson Chi Square test) (**Table 2**).

Table 2 The association of type 2 MI with clinical parameters.

	Type 2 MI	Non type 2 MI	p value
Age (y)	78.73 ± 11.17	71.55 ± 14.76	<0.05
Men	257	685	
Women	243	566	0.23
DM	34/500	118/1251	0.07
RF	67/500	98/1251	<0.05
Mortality	193/500	336/1251	<0.05

RF-Renal failure, DM-Type 2 Diabetes Mellitus Type 2 MI-Type 2 myocardial infarction

A significant difference was found between patients who had renal failure and type 2 MI (67 patients out of 500, 13.4%), compared with 98 patients with renal failure but without type 2 MI out of 1251 (7.84%) (p<0.05) (Pearson Chi Square) (**Table 2**).

5 years mortality rate post hospitalization was significantly higher among patients with type 2 MI. 193 patients with type 2 MI (out of 500) died during the follow-up period (38.6%) compared with 336 patients out of 1251 (26.8%) who died at that period of time who did not have MI during hospitalization with CAP (p<0.05) (Pearson Chi Square test) (**Table 2**).

Mortality during 5 years after discharge from the hospital

Gender did not affect 5 years mortality rate post discharge from the hospital (294 men died and 648 survived, while 235 women died and 574 survived during the time of follow-up (p=0.326, Pearson Chi Square) (**Table 3**).

Table 3 Characteristics of patients who died during the follow-up.

	Died	Survived	p value
Men	294	648	
Women	235	574	0.326
DM	481	1118	
No DM	48	104	0.701
RF	84	81	
No RF	445	1141	<0.05
Age (y)	77.80 ± 12.18	71.78 ± 14.63	<0.05

RF-Renal failure, DM-Type 2 diabetes mellitus, Type 2 MI-type 2 myocardial infarction

No difference was observed in mortality rate among patients with type 2 DM-481 diabetic patients died and 1118 survived, while 48 non-diabetic patients died and 104 survived during the 5 years follow-up period post hospitalization (p=0.701, Pearson Chi Square) (**Table 3**).

A total of 84 patients with renal failure died and 81 patients survived 5 years following hospitalization, while 445 patients without renal failure died and 1141 patients without renal failure survived during the 5 years follow-up period post hospitalization (p<0.05, Pearson Chi Square) (**Table 3**).

Age was another independent variable that affected death. Older patients had a higher mortality rate (77.80 ± 12.18 years old vs. 71.78 ± 14.63 years old, p<0.05) (**Table 3**).

Type 2 MI and mortality rate 5 years post discharge

Logistic regression analysis was used to examine the relationship between type 2 MI and mortality rate among patients admitted with CAP up to 5 years after hospitalization. Death was the dependent variable, and the independent variables included type 2 MI, age, gender, type 2 DM, and renal failure. Based on the model used (Hosmer and Lemeshow; X²=7.372, p>0.05) type 2 MI predicted a higher mortality rate during the 5 years follow-up post discharge with odds ratio of 19.90. We also found that patients with renal failure had a higher mortality rate with odds ratio of 2.054.

Discussion

We found that patients admitted with CAP who developed type 2 MI had a 19.90 fold increased mortality rate during the 5 years follow-up period after discharge from hospitalization. Older age and renal failure were independent variables that affected the mortality rate.

Patients who suffer myocardial infarction without electrocardiographic changes represent a different kind of myocardial infarction called type 2 myocardial infarction (type 2 MI). The mortality rate of patients who suffer type 2 MI is high reaching almost 50% after 2 years [11]. Among hospitalized patients with CAP acute myocardial infarction was the second most common etiology associated with clinical failure following severe sepsis. Patients with type 2 MI are less likely to undergo coronary revascularization or to be treated with dual anti-platelet therapy, statins, and beta blockers than patients with type 1 myocardial infarction [11]. Previous studies that investigated the prevalence of increased troponin level in association with pneumonia found a higher in hospital mortality rate in patients with increased troponin levels [10,11]. A prospective study that followed 474 patients admitted with CAP found that raised troponin level predicted 30 day mortality in age adjusted analysis [12].

Our study is the first one that describes a long term follow-up mortality rate after hospitalization of patients with CAP.

The mechanism is not clear but it could be that cardiac involvement may be an under-recognized determinant of death in patients admitted with CAP, and patients with cardiac involvement may need a different management and care.

Systemic inflammatory response that leads to severe sepsis is a known mechanistic pathway leading to severe inflammatory response syndrome in patients admitted with pneumonia. The burst of inflammatory response causes activation of the endothelial cells, leading to endothelial dysfunction with activation of the pro-inflammatory system, plaque rupture, and the development of acute myocardial infarction [13,14]. A possible explanation could be an oxidative stress that leads to myocardial infarction and necrosis during the acute phase of pneumonia. A prospective study that studied 135 patients with CAP found that 54% of the admitted patients had elevated serum levels of troponin [15,16]. Serum NOX2 derived protein peptide (a marker of NOX2 activation) was linearly correlated with troponin level, and provided an insight to a possible mechanistic link between pneumonia and cardiac damage. It could be that NOX-2 derived oxidative stress may be implicated in myocardial injury and inhibition of this pathway may protect against the free radicals' phenomenon [16].

Study limitations: the study was a retrospective study, which limits the ability to conclude firm conclusions. In order to consolidate our findings the same kind of study should be performed but in a prospective design, so that firm conclusions and clinical implications could be adopted.

In summary, this study showed that mortality rate during 5 years after hospitalization of patients admitted with CAP who developed type 2 MI was significantly higher compared with

patients without type 2 MI during hospitalization. We recommend to add troponin level to the risk stratification panel of patients admitted with CAP and to consider type 2 MI as a risk factor for mortality of patients admitted with CAP, especially for older patients and those who suffer from renal failure. Adding type 2 MI to the risk stratification of patients admitted with CAP may change our management policy, and may lower mortality rate after hospitalization of patients at risk by appropriate interventions and care.

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