

## Causes of mortality in a department of cardiology over a 15-year period

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### ABSTRACT

**Aims:** Over the last four decades, in-hospital mortality from acute coronary syndromes (ACS) has declined. We characterized the patients who died in our cardiovascular intensive care unit (CICU) over a 15-year period. Based on these data, we described the changing patient population in the CICU.

**Methods:** This retrospective study compared characteristics of patients who died in our CICU in 2005–6, 2013–4 and 2019. During these 5 years, 13,931 patients were hospitalized; 251 (1.8%) died. The mean age of the patients who died was 76 years, 144 (57%) were men. ACS was the leading cause of admission (93 patients, 37%), and 145 (58%) patients had a history of heart failure prior to hospitalization. The leading cause of death was cardiogenic shock in 104 (41%) patients, septic shock in 48 (19%) patients, and combined cardiogenic and septic shock in 31 (12%). Patients hospitalized in the later years of the study were significantly older (67.7, 69.0 and 70.5 years, 2005–6, 2013–4 and 2019, respectively,  $p < 0.02$ ) but their medical characteristics did not differ significantly between the years examined.

**Conclusions:** The profile of the patients who died did not change significantly over the 15-year study period. Age of admitted patients was higher in later years of the study. The leading cause of admission was ACS and the leading causes of death were cardiogenic and septic shock. Based on our observations, additional skills should be added to the curriculum of cardiology, including the management of patients with multiorgan failure.

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## 1. Introduction

Major advances in cardiology over the last four decades have resulted in substantial changes in clinical practice in departments of cardiology [1,2]. In addition, increases in both longevity and in the prevalences of chronic diseases have changed the profile, treatment, and prognosis of hospitalized patients [3–7]. In previous decades, patients with acute coronary syndromes (ACS) demanded the most resources in departments of cardiology, due to complications of ACS such as heart failure. Over the last three decades, patients with ACS who undergo early revascularization have required relatively fewer resources and are generally discharged 48–72 h of admission [1,8]. With early revascularization and pharmacological treatment, younger patients with ACS rarely die during the acute event or in the subsequent years. Accordingly, most resources are currently allocated to older patients with multiple

co-morbidities such as renal failure, heart failure and arrhythmias [2,8]. Hence the cardiovascular intensive care unit (CICU) has taken on a new role [9]. In-hospital mortality has become low, for ACS patients in general, and specifically for patients with ST-elevation myocardial infarction (STEMI) who undergo revascularization [10]. We recently showed a higher mortality rate among patients with ACS who did not undergo coronary angiography than among those who underwent such procedures [11]. We also found that older STEMI patients with multiple comorbidities tend to arrive late to the hospital and to have worse prognosis, while mortality in our entire STEMI patient population has reached as low as 5% [10].

The current study was set to characterize patients who die in our CICU. These patients represent the far end of the spectrum of the patient population. Analyzing the dynamics of this subpopulation over 15 years can provide invaluable information, and insights for improving resource allocation.

## 2. Methods

The Lady Davis Carmel Medical Center is a medium size hospital (500 beds) located in Haifa, Israel, and is part of the Clalit Health

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Systems organization. The Department of Cardiovascular Medicine admits patients from the emergency room and from community-based outpatient clinics run by the department cardiologists [12]. The department is composed of 16 intensive care beds (CICU), 16 monitored beds (step-down) and 8 monitored beds that are used only during weekdays. Patients in severe condition are cared for in the CICU beds of the department. During the study period, patients who deteriorated in our regular department were transferred to the CICU. Therefore, all the death events occurred in the CICU, with the exception of very few patients whose deaths were declared in the catheterization laboratory.

We studied the files of the patients who died in the years 2005–6, 2013–4 and 2019, and for whom we had full data sets. We started from 2005 to 6, as this marks the initiation of electronic patient files in our department. For each patient, a demographic profile, presenting symptoms, events during hospitalization, comorbidities and cause of death were recorded. Each file was reviewed by one researcher. For patients for whom the researcher was unable to determine the cause of death, a second, and sometimes a third researcher, co-reviewed the file (40% of the files were reviewed by at least two researchers). Data were recorded using Microsoft excel. The institutional review board approved the study protocol.

### 2.1. Statistical methods

Continuous data are presented as means  $\pm$  standard deviations (SD), and categorical variables as numbers and percentages.

We compared data of patients who died during three periods: 2005–6, 2013–4 and 2019. For categorical variables, we used the chi square or exact test for small samples.

The results were considered statistically significant for 2-sided  $P < 0.05$ .

SPSS version 24.0 was used to perform all the statistical analyses.

To compare the male-to-female ratio between the patients admitted and those who died, we applied the chi square goodness of fit test to calculate observed and expected frequencies in each gender category.

## 3. Results

During the 5-year study period, 13,931 patients were hospitalized in the Department of Cardiovascular Medicine. Of them, 251 (1.8%) died (Fig. 1). Complete data of 251 patients were available for the analysis: 95 who died in 2005–6, 111 who died in 2013–4, and 45 who died in 2019.

The mean age of the patients who died was 76 years, 144 were men (57%). ACS was the leading cause of admission (93 patients, 37%); 145 (58%) patients had a history of heart failure prior to hospitalization (Table 1). The mean age of the patients hospitalized in our department increased over the three time periods tested: 67.7, 69.0 and 70.5 years (2005–6, 2013–4 and 2019, respectively), a change that was statistically significant ( $p < 0.02$ ). The mean age of the patients who died in each period was significantly higher than that of the age of the entire group of patients hospitalized (Table 1).

The male-to-female ratio changed over the three periods, with a reduction in male majority over time (69.4%, 68.2% and 66.1%, respectively,  $p = 0.009$ ). Females comprised a greater proportion of the patients who died than of those who were admitted (Table 1). Of the patients hospitalized in our department, 67.8% were men and 32.2% women. We expected that this gender proportion would be observed among the patients who died. However, among the patients who died, 57.4% were men and 42.6% women.

This difference in gender proportion was statistically significant. The number of men who died was lower than expected ( $n = 144$  vs.  $n = 171$ ) while the number of women who died was higher than expected ( $n = 107$  vs  $n = 80$ ), ( $p < 0.0001$ ). The mean age of admitted women was higher than the mean age of admitted men, 69.6 compared to 65.7 years ( $p < 0.001$ ), as was the age of women who died compared to men who died, 79.1 vs. 74.3 years ( $p < 0.001$ ). There were no significant differences between patients admitted in years 2005–6, 2013–4 and 2019 (Table 1). Rates of hypertension, diabetes, and a history of coronary artery disease prior to admission were high, and similar throughout the study period (Table 1). The proportion of patients with implantable cardioverter defibrillators was higher, without statistical significance, in the year 2019 (Table 2).

Over the 15-year study period, the proportion of patients who underwent percutaneous coronary interventions, the occurrence of heart failure and the use of counter pulsation intra-aortic balloon pump did not change (Table 2). The leading cause of death was cardiogenic shock in 104 (41%) patients, septic shock in 48 (19%) patients, and combined cardiogenic and septic shock in 31 (12%) (Table 2). Although the proportion of patients that died of combined cardiogenic and septic shock was significantly higher in the earlier period, the numbers are small and no definite conclusions can be drawn (Table 2). Renal and respiratory failure as the cause of death was reported in 15 patients. Other causes of mortality that are not presented on Table 2 were mesenteric events (2 patients), pulseless electrical activity with no apparent cause (3 patients), tamponade (5 patients), complication during interventional procedures (3 patients), and cancer (3 patients).

## 4. Discussion

In the current study, we showed that patients who died in the CICU are generally elderly, with multiple comorbidities and a history of heart failure, and that they succumb mostly to cardiogenic and septic shock. In the later years, a significantly greater proportion of patients had a history of heart failure and a lower proportion had ACS as the primary cause of admission, but this latter difference did not reach statistical significance.

The evolution of coronary care units since their inception in the early 1960s was dictated by the epidemiology of heart disease, and the available technology and therapeutics [2,8,13]. While during the 1960s, 1970s and early 1980s, treatment was focused on the detection and prevention of arrhythmias, treatment of complications of acute myocardial infarction dominated the next 20 years [2]. Over the last two decades, larger and less homogenous patient populations have been hospitalized in the CICU. Older patients with multiple comorbidities currently comprise most of the hospitalized patients in the CICU, both in low and high-volume cardiac hospitals [14]. Due to the common performance of early revascularization, patients with STEMI have become a subpopulation in the CICU that requires relatively little attention. Patients with non-STEMI, patients with exacerbation of chronic heart failure, and patients with severe arrhythmias and sepsis, all with additional comorbidities, constitute the majority of those hospitalized in the CICU. These patients require most of the resources, and have the highest rates of mortality [15].

Over the 15-year study period, ACS decreased as a diagnosis at admission among the patients who died in-hospital: from 43% to 29%. This concurs with the findings of other studies [15,16]. The majority of patients who died in the CICU during all three periods of our study were diagnosed with cardiogenic or septic shock, or a combination of cardiogenic and septic shock. Combined septic and cardiogenic shock was determined as the cause of death for a higher proportion of patients in the first than the later years of

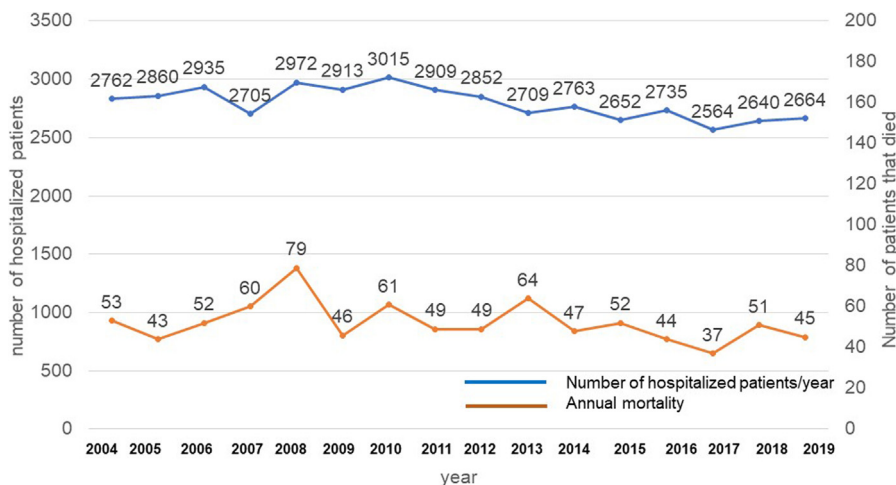


Fig. 1. number of hospitalized patients in or department every year from 2005 to 2019 and number of patients that died every year.

**Table 1**  
Demographic characteristics and comorbidities of patients hospitalized in a department of cardiovascular medicine in three periods of time over a total of 15 years.

	Years 2005–6 n = 95	Years 2014–5 n = 111	Year 2019 n = 45	p value
Age (mean) years	76 ± 11	76 ± 12	77 ± 13	0.9
Male/Female	54/41	63/48	27/18	0.9
History of heart failure (%)	50(53%)	69(62%)	26(58%)	0.39
Diabetes (%)	40(42%)	60(54%)	25(56%)	0.16
Hypertension (%)	71(75%)	92(83%)	39(87%)	0.17
Active smoking (%)	10(11%)	13(12%)	6(13%)	0.87
History of coronary heart disease prior to the index hospitalization (%)	58(61%)	58(52%)	25(56%)	0.44
With an implantable cardioverter defibrillator (%)	7(7%)	13(12%)	9(20%)	0.09

**Table 2**  
In-hospital course of patients hospitalized in a department of cardiovascular medicine in three periods of time over a total of 15 years.

	Year 2005–6 n = 95	Year 2013–4 n = 111	Year 2019 n = 45	p value
Hospitalization length (mean) days	7.9 ± 10.3	8.5 ± 11.4	6.5 ± 6.9	0.55
<b>Admission diagnosis:</b>				
STEMI (%)	22(23%)	18(17%)	8(18%)	0.42
Non-STEMI (%)	21(22%)	19(17%)	5(11%)	0.27
Arrhythmia (%)	8(8%)	18(16%)	5(11%)	0.22
Heart failure (%)	24(25%)	26(23%)	17(38%)	0.17
Sepsis (%)	4(4%)	5(5%)	0	0.37
Other	16(17%)	24(22%)	7(16%)	0.59
<b>In-hospital course:</b>				
PCI (%)	21(22%)	31(28%)	12(27%)	0.60
Heart failure (%)	50(53%)	69(62%)	26(58%)	0.39
Use of IACP (%)	22(23%)	26(23%)	5(12%)	0.19
Atrial fibrillation (%)	24(25%)	40(36%)	14(31%)	0.25
<b>Cause of death:</b>				
Septic shock (%)	13(13.7)	25(22.5%)	10(22.2%)	0.23
Cardiogenic shock (%)	39(41.1%)	42(37.8%)	23(51.1%)	0.31
Cardiogenic and septic shock (%)	20(21.1%)	10(9.0%)	1(2.2%)	0.002
Asystole or arrhythmia (%)	6(6.3%)	6(5.4%)	0(0)	0.24
Hemorrhage (%)	1(1.1%)	3(2.8%)	3(6.7%)	0.19
Cerebrovascular event	1(1.1%)	2(1.8%)	0(0.0%)	0.81
Pulmonary emboli	1(1.1%)	1(0.9%)	1(2.2%)	1.0
Renal failure	1(1.1%)	5(4.5%)	1(2.2%)	0.36
Respiratory failure	3(3.2%)	4(3.6%)	1(2.2%)	1.0
Dead on arrival	3(3.2%)	4(3.6%)	1(2.2%)	1.0

STEMI: ST-elevation myocardial infarction; PCI: percutaneous coronary interventions; IACP: intra-aortic counter pulsation balloon.

our study. However, the total proportions of death due to septic shock did not differ significantly between the periods (30% for 2005–6, 30% for 2013–4 and 24% for 2019). Regarding less common causes, we identified patients who died of pulmonary emboli, dissection of the aorta and cerebrovascular events. For a substantial

number of patients, respiratory and renal failure were the main causes of death, most of these had had concomitant heart disease. We also included in our reported, mortality due to complications of catheterizations and deaths due to tamponade. Such a profile of dying patients is also common in regular intensive care units

[17]. The management of these patients with multiple organ failure requires skills that surpass those that are imparted in the cardiology curriculum. Teaching resident physicians in the management of patients on respirators was shown to improve patients' outcomes [18,19]. Several models have been implemented to operate CICU, such as the inclusion of an intensivist in the CICU team, and reliance on consultations, as needed, with the intensive care staff [8]. Another substantial group of our patients arrived under resuscitation to the CICU, from either the emergency room or from ambulance services. We were able to return circulation for short periods of time, but the patients died within 2 h of arrival. The exact cause of death could not be determined, and they were classified as dead on arrival. We encourage ambulance services and emergency room staff to become involved in patients who arrive under resuscitation, with the presumption that they can be saved using extracorporeal membrane oxygenator (ECMO).

The mean age of the patients admitted was older in later years, and the proportion of women was higher among the patients who died than among all the admitted patients. This phenomenon is well known, as women admitted to departments of cardiology tend to be older and to have worse prognosis [20].

The use of intra-aortic counter pulsation balloon (IACPB) in patients in the CICU was less common, though without statistical significance, during the most recent year of the study period. This is despite the greater proportion of patients with heart failure, and may reflect guideline recommendations on the use of IACPB [21]. Occurrences of atrial fibrillation and arrhythmias were common, and in some patients were the cause of death. Atrial fibrillation and lethal arrhythmias are common in patients with heart failure and shock. Some changes in cause of death may be attributed to changes in the philosophy of patients, families, physicians and the Israeli law, which in more recent years have allowed patients to die peacefully when overwhelming clinical circumstances are present [22,23]. We identified three patients who died due to advanced cancers, although the final events were asystole or pulseless electrical activity; these were classified as cancer-related mortality.

In summary, analysis of the patient profile, the in-hospital course and causes of death of patients who died in our CICU over 15 years showed that patients were generally elderly, and that ACS was the reason for admission in only 29% in the year 2019. Based on our observations, additional skills should be added to the curriculum of cardiology, including the management of patients with multiorgan failure.

## 5. Ethics approval and consent to participate

The institutional review board of Lady Davis Carmel Medical Center waived the need for approval of this study.

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There are no funding resources.

## Declaration Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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