The “Burden” of Malignancy in a Tertiary Hospital Intensive Cardiovascular Care Unit

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Abstract

Objectives: During the past decade, the most common causes of mortality and morbidity were cardiovascular diseases and malignancies. The aim of the current study was to describe the incidence, course of admission, and short-term (30-day) prognosis of patients with and without malignancy, admitted to a tertiary center intensive cardiovascular care unit (ICCU). **Methods:** A prospective observational study of 2,259 patients admitted to the ICCU was conducted between January 2014 and December 2015. Patients with malignancies ($n = 256$) were divided into 2 groups: those with solid and those with homogenous tumors. **Results:** The time of diagnosis was categorized into 3 patient groups: recent (<6 months), 59 patients (23%); late (6–24 months), 49 patients (19%), and very late (>24 months), 148 patients (58%). Those with a history of malignancy were older (73 ± 12 vs. 64 ± 15 , $p < 0.001$) and were more likely to be female ($p = 0.002$). After using a multivariate logistic regression model analysis, no differences were found in therapeutic interventions and clinical outcomes, including major bleeding and acute renal failure, between patients with and without malignancies.

Conclusions: Patients with a malignancy comprised about 10% of the entire ICCU population. While mortality was independently associated with advanced age, renal failure, and a diagnosis of ST-elevation myocardial infarction, malignancy alone was not found to be independently associated with a higher mortality rate at 30 days of follow-up.

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Introduction

During the past decade the most common causes of mortality and morbidity were cardiovascular diseases and malignancies [1–4], both of which share several similar risk factors, such as aging and smoking. Technological development and improved medical treatments have dramatically increased life expectancy. New pharmacological approaches combined with surgery and radiotherapy can prolong survival in cancer patients. Unfortunately, research has shown that these treatment modalities could be the underlying causes behind various cardiovascular

diseases [5, 6]. Key examples are anthracycline treatment for cancer, which could cause irreversible cardiomyopathy, and thorax radiotherapy, which could induce coronary artery disease [7]. While in the past acute coronary syndrome (ACS) was the major cause of mortality, cancer is now becoming the leading cause of death in the Western world [1–3]. Thus, it is not uncommon to meet cancer patients in cardiology wards due to their various cardiovascular diseases. In 2012, Yusuf et al. [8] described the outcome of ST-elevation myocardial infarction (STEMI) and non-STEMI in patients suffering from malignancies. Because these patients had been treated with aspirin and beta-blockers, their chances of survival had improved. In another recent study, Al-Kindi and Oliveira [9] found that the prevalence of coronary artery disease ranges from 5.7% in patients with breast malignancy to 20.8% in patients with lung malignancy.

The aim of the current study was to describe the incidence, course of admission, and short-term prognosis of patients with and without malignancy, admitted to a tertiary center intensive cardiovascular care unit (ICCU).

Methods

A prospective observational study was conducted between January 2014 and December 2015 in the ICCU of the Sheba Medical Center, which is a tertiary center handling approximately 192,000 emergency department visits per year, with >94,000 admissions annually. The inclusion criteria comprised all patients admitted to the ICCU, while exclusion criteria were: (1) patients under the age of 18 years; (2) pregnant women; (3) patients with psychiatric conditions, and (4) patients with any other condition requiring chronic nursing care.

Data Collection and Patient Allocation

Data were collected from patient charts and interviews. Independent variables included age, gender, smoking, a chronic illness (hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, and heart failure), debilitation (denoting or characteristic of a morbid process that causes weakness and the need for assistance in daily activities), previous percutaneous coronary intervention (PCI), and previous coronary artery bypass graft (CABG). The admission course included: PCI, CABG, the insertion of an arterial line, intubation, mildly induced hypothermic treatment, use of intravenous inotropes, the insertion of an intra-aortic balloon pump, extracorporeal membrane oxygenation, insertion of a pacemaker, blood transfusions, and cardiopulmonary resuscitation. Complications during hospitalization included: acute renal failure, shock, arrhythmias, cerebrovascular accidents, infection, bleeding, acute myocardial infarction, urgent revascularization, and death. Mortality at 30 days was obtained from the Israeli Ministry of Health Registry.

Patients with malignancies were divided into 2 groups: those with solid and those with homogenous tumors. The time of diag-

Table 1. Basic patient characteristics

	Malignancy (n = 256)	Non-malignancy (n = 2,003)	p value
Female gender, %	35.5	26.4	0.002
Age, years	72.94 ± 12.51	64.18 ± 15.01	<0.001
Hospitalization length, days	3.24 ± 2.43	3.01 ± 3.80	0.340
COPD, %	12.9	11.7	0.586
Cerebrovascular accidents, %	11.7	10.6	0.579
Renal failure, %	24.2	15.5	<0.001
Diabetes mellitus, %	32.4	26.3	0.009
Pulmonary hypertension, %	5.5	3.7	0.167
Anemia, %	18.8	9.5	<0.001
Cognitive decline, %	5.5	4.7	0.583
Debilitation, %	14.1	9.1	0.012
Prior coronary artery disease, %	37.1	36.1	0.758
Prior congestive heart failure, %	16.8	18.0	0.646
AICD/CRT-D, %	9.9	9.0	0.674

COPD, chronic obstructive pulmonary disease; AICD, automated intra-cardiac defibrillator; CRT-D, cardiac resynchronized therapy defibrillator.

Fig. 1. Time from diagnosis to malignancy: recent, late, and very late.

nosis was categorized into 3 groups: recent (up to 6 months); late (6–24 months), and very late (>24 months). Patients with both types of tumors, who had been diagnosed at different times, were grouped according to their last diagnosis.

Statistical Analysis

Continuous variables are presented as means ± standard deviation, and the *t* test was used for comparison of these variables. Categorical variables are presented as percentages and were compared by χ^2 or Fisher exact test as indicated. The primary end points were further analyzed using multivariate logistic regression adjusted for age, gender, renal failure, diabetes mellitus, and admission due to STEMI. *p* < 0.05 was considered statistically significant. Statistical analysis was performed with SPSS v.20.0 software (SPSS Inc., Chicago, IL, USA).

Table 2. Major causes of admission

	Malignancy (<i>n</i> = 256), %	Non- malignancy (<i>n</i> = 2,003), %	<i>p</i> value
ACS	52.5	61.2	0.008
STEMI	19.6	26.7	0.015
Non-STEMI	23.0	26.9	0.184
Type II myocardial infarction	9.8	5.5	0.007
Severe congestive heart failure	17.2	15.9	0.602
Ischemic cardiomyopathy	10.2	11.0	0.691
Nonischemic cardiomyopathy	5.1	3.3	0.158
Valvular cardiomyopathy	3.5	2.3	0.257
Postprocedure	15.2	14.4	0.712
Post-TAVI	11.3	7.1	0.016
Postelectrophysiology procedure	2.0	3.8	0.136
Postcatheterization	1.2	2.7	0.134
Arrhythmias	22.3	17.6	0.069
Tachycardia	11.7	10.0	0.401
Bradycardia	11.7	6.6	0.003
Out-of-hospital sudden cardiac death	2.3	2.7	0.742
Pulmonary emboli	9.4	3.4	<0.001
Myocarditis	1.2	3.4	0.051
Tamponade	3.5	2.1	0.169
Apical ballooning (Takotsubo)	1.2	0.7	0.406
Shock	8.6	7.5	0.548
Valvular disease	5.9	3.4	0.054
Sepsis	3.5	2.1	0.169

ACS, acute coronary syndrome; STEMI, ST-elevation myocardial infarction; TAVI, transcatheter aortic valve implantation.

Results

Of the 2,259 patients admitted to the ICCU during the study period, 256 (11.33%) were diagnosed with a malignancy. Of them, 206 (80%) had a solid type and 50 (20%) had a homogenous type of malignancy. Fifty-nine (23%) patients had a recent diagnosis, 49 (19%) had a late diagnosis, and 148 (58%) had a very late diagnosis (Fig. 1).

Patient Characteristics

The patient characteristics are presented in Table 1. Patients with a history of malignancy were older (73 ± 12 vs. 64 ± 15 , $p < 0.001$), tended to be female (35.5 vs. 26.4%, $p = 0.002$), suffered more from anemia (18.8 vs. 9.5% $p < 0.001$) and renal failure (24.2 vs. 15.5%, $p < 0.001$), and were more debilitated (14.1 vs. 9.1%, $p = 0.012$) compared with patients without a history of malignancy.

Major Causes of Admission

The major causes of admission are presented in Table 2. Patients with a history of malignancy were more frequently hospitalized due to bradycardia (11.7 vs. 6.6%,

Table 3. Course of hospitalization and complications

	Malignancy (<i>n</i> = 256), %	Non- malignancy (<i>n</i> = 2,003), %	<i>p</i> value
Primary PCI	14.8	22.7	0.004
PCI	17.6	20.3	0.307
CABG	2.3	3.2	0.459
Catheterization	16.4	14.0	0.296
Intra-aortic balloon pump	2.0	2.3	0.728
ECMO	0	0.01	1.0
Mechanical ventilation	7.8	10.1	0.251
Hemodialysis	2.7	2.4	0.779
Pacemaker/ICD	11.3	8.8	0.191
Ventricular tachycardia ablation	0.8	1.5	0.361
Electrophysiology study	0	0.2	0.676
<i>Complications</i>			
Blood transfusion	6.3	5.0	0.390
Thrombolysis	1.6	0.3	0.028
Inferior vena cava filter	0	0.3	0.468
Cardiopulmonary resuscitation	2.0	3.3	0.247
Hypothermia (MTH)	1.2	1.8	0.441
Amines	16.1	13.2	0.227
Arterial line	31.4	24.8	0.003
Direct current shock	2.7	6.3	0.031
CHF – during stay	15.2	14.9	0.894
Shock – during stay	7.0	6.6	0.812
Remyocardial infarction	1.2	1.0	0.794
Arrhythmia	5.1	4.4	0.644
Mechanical complication	1.6	2.1	0.569
Infection	3.9	3.6	0.833
CVA – during stay	0	0.9	0.114
Bleeding	3.5	3.4	0.919
Acute renal failure	12.9	9.5	0.085

More than 1 complication could be attributed to a patient. PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; ECMO, extracorporeal membrane oxygenation; ICD, intracardiac defibrillator; MTH, mild therapeutic hypothermia; CHF, congestive heart failure; CVA, cerebrovascular accidents.

$p = 0.003$), pulmonary emboli (9.4 vs. 3.4%, $p < 0.001$), and post-transaortic valve implantations (TAVI; 11.3 vs. 7.1%, $p = 0.016$) compared with patients without a history of malignancy. However, those with a history of cancer were less likely to be admitted because of ACS (52.5 vs. 61.2%, $p = 0.008$), especially due to acute STEMI (19.6 vs. 26.7%, $p = 0.015$), although more patients were admitted with a diagnosis of type II myocardial infarction (9.8 vs. 5.5%, $p = 0.007$).

Hospitalization Course and Complications

During hospitalization both groups underwent coronary angiography at similar rates (16.4 vs. 14.0%, $p = 0.296$), as well as PCI (17.6 vs. 20.3%, $p = 0.3$), CABG (2.3 vs. 3.2%, $p = 0.457$), and intra-aortic balloon pump inser-

Table 4. Mortality rate of patients with and without malignancy

	Malignancy (<i>n</i> = 256), %	Non- malignancy (<i>n</i> = 2,003), %	<i>p</i> value
Mortality	5.5	2.5	0.008
Mortality at day 7	7.0	3.2	0.002
Mortality at day 30	10.2	5.6	0.004

tion (2.0 vs. 2.3%, $p = 0.728$). Complication rates (acute renal failure, bleeding, arrhythmias, shock, acute heart failure, and cerebrovascular accidents) were similar in both groups, except for the need for direct current shock, which was more frequent in the nonmalignancy group (2.7 vs. 6.3%, respectively, $p = 0.031$; Table 3).

Mortality Rate

The mortality rate was higher in the malignancy group during hospitalization (5.5 vs. 2.5%, $p = 0.007$) and at day 30 (10.2 vs. 5.6%, $p = 0.004$; Table 4). There was no difference in the mortality rate between subgroups of homogeneous versus solid types of tumors. During the first week of admission the mortality rate was higher among patients with a recent diagnosis of malignancy compared with patients with a very late diagnosis (14.0 vs. 4.7%, respectively, $p = 0.017$). A similar mortality rate was seen at day 30 (17.5 vs. 6.7%, respectively, $p = 0.014$; Fig. 2). Nevertheless, after using a multivariate logistic regression model analysis, malignancy was not independently associated with a higher mortality rate at day 30. A higher mortality rate was independently associated with advanced age (OR 1.03, 95% CI 1.02–1.05), renal failure (OR 3.45, 95% CI 2.23–5.34), and a diagnosis of STEMI (OR 2.20, 95% CI 1.44–3.76).

Discussion

Our study is one of the first of its kind to describe the contemporary trend in patients admitted to the ICCU. While cardiovascular disease and malignancy are the leading causes of mortality in the Western world, information regarding the prognosis of patients with malignancy admitted to the ICCU is scarce. Several differences were found between patients with and without malignancy who were admitted to the ICCU. Patients with malignancy were older, tended to be female, suffered from anemia and renal failure, and were generally more

Fig. 2. Kaplan-Meier curve: 30-day mortality according to the time of malignancy diagnosis.

debilitated. Patients with malignancies suffered more from bradycardia, pulmonary embolism, and post-TAVI. On the other hand, nonmalignancy patients suffered more from ACS, and especially acute STEMI. Nevertheless, the rates of coronary angiography, PCI, and CABG were similar in both groups. ICCUs are no longer reserved solely for ACS patients [10, 11]. As life expectancy increases and populations become older, Western medicine faces new challenges. One of these is the treatment of cardiovascular patients who are becoming older with more complex valvular diseases, arrhythmias, and malignancies [12]. As a result, these patients are being admitted to the ICCU for numerous causes, as was shown in our study. Once admitted to the ICCU, physicians are faced with the dilemma of treating these patients with invasive procedures versus conservative therapy, which is often less favorable [13]. A recent study compared the results of TAVI in cancer and noncancer patients, and found no difference between the 2 groups with regard to their outcomes [14]. In accord with our findings, about 10 percent of patients with malignancies underwent TAVI, and none of them died at 30 days of follow-up. In our study, the mortality rate at days 7 and 30 of follow-up was higher mainly in elderly patients and in those with STEMI at presentation, and not due to malignancy. Moreover, there was no difference in mortality regarding the type of malignancy. When comparing patients with a recent versus late diagnosis of malignancy, the former group was more prone to worse major adverse cardiac

events including mortality, although in a multivariate analysis this trend was not seen.

Our findings correlate with other studies [15–17] which examined the outcomes of STEMI in cancer patients. Cancer patients were older and included more females and those who suffered more from anemia. In accord with our findings, another study by Kurisu et al. [18], who followed up 18 cancer patients and 59 noncancer patients following PCI for acute myocardial infarction, found that there was no difference in in-hospital mortality between the groups.

Limitations

There are several limitations to our study. First, there might have been a selection bias, since patients with a more aggressive, advanced stage of cancer were probably not admitted to our department, although in cardiac emergencies such as STEMI all patients were admitted to our ICCU. Second, this was a single center study. Lastly, our follow-up was limited to 30 days. Nevertheless, the

main purpose of our study was to examine the short-term outcomes of acutely ill cancer patients in the ICCU.

In conclusion, our study represents a new era, comprising an older patient population with more complex conditions, including malignancies, who were admitted to a tertiary ICCU. Previous reports have dealt mainly with community-based cohorts. Our study is the first to demonstrate the incidence of patients with malignancy admitted to an ICCU. These patients represent more complex cases and are admitted due to a variety of reasons. Nevertheless, according to our findings, although these patients represent more challenging methods of treatment and medical dilemmas, it seems that they can benefit, at least in the short term, from full medical treatment, including invasive procedures. Moreover, our study is also the first to provide information regarding the complication rate in these patients, which was not higher in comparison with the other ICCU patients without malignancy. Further long-term trials with larger cohorts are warranted in order to better characterize this subgroup of patients.

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