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VIEWPOINT

Impact of Cardiopulmonary Resuscitation on Survival in Cancer Patients

Do Not Resuscitate Before or After CPR?

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Cancer patients have particularly low rates of return of spontaneous circulation (ROSC) and survival to hospital discharge following cardiopulmonary resuscitation (CPR) compared with non-cancer patients (1). The quality of life at discharge of those who survive after CPR is often diminished, and a significant percentage survive for only a short time following discharge (2). Among survivors, there is a high likelihood of changing their code status to do not resuscitate (DNR) post-cardiac arrest. Although variations in the rates of survival to hospital discharge have been identified in different cancer patient populations (e.g., pediatric vs. adult patients, patients with solid vs. hematological malignancies, patients with metastatic vs. nonmetastatic disease), the use of CPR has largely been indiscriminate (3,4). More efforts are needed to identify the specific cancer patient populations that would benefit in terms of survival to hospital discharge. In our view, there is a need to systematically assess whether the available CPR measures are futile, to avoid potential painful and costly interventions that do not benefit the patient.

To help understand this topic, we sought to identify cancer patients with a poor prognosis who might benefit from an early discussion of end-of-life measures and further treatment goals before the occurrence of sudden, unanticipated cardiac arrest. We conducted retrospective analyses of 650 patients (>18 years of age) who experienced in-hospital cardiac arrest between January 2011 and December 2015 at The University of Texas MD Anderson Cancer Center, Houston, Texas. Cardiac arrest was defined by the presence of hemodynamically unstable cardiac rhythm (ventricular tachycardia, ventricular fibrillation, cardiac asystole, or pulseless electrical activity). The patients were identified by using a CPR database provided by ZOLL Medical Corporation (Chelmsford, Massachusetts). The study protocol was approved by the local institutional review board.

Patients were excluded from the study if they did not have a cancer diagnosis or if they did not experience cardiac arrest. The patients' pre-cardiac arrest clinical characteristics (age, sex, type of malignancy, and cardiovascular risk factors such as history of smoking, hypertension, hyperlipidemia, and cardiovascular disease) were reviewed. CPR was considered effective if it met the 2015 American Heart Association recommendations for compression rate (100 to 120 compressions/min), depth (2.0 to 2.4 cm), and fraction (60% to 80%). All CPR team members were trained and certified in advanced cardiac life support techniques. Real-time measurements of the average

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chest compression rate, average compression rate, average compression depth, and overall compressions in the targeted zone were obtained by using ZOLL Medical Corporation equipment. The CPR database only included patients who were full code at the time of study inclusion. The database did not include information on whether the DNR decision was made by the patient or medical power of attorney. Descriptive statistics were used to summarize the data and to describe the outcomes. Categorical variables are presented as frequencies (percentages), and survival rate is presented with 95% confidence intervals. The analysis was performed with Pandas and Lifelines packages for Python, and Microsoft Excel (Microsoft, Redmond, Washington) was used to summarize and tabulate the results.

Table 1 presents a summary of the clinical characteristics of the patients. The mean age was 56 ± 17 years, 73.2% were >50 years of age, and 53.7% were male. Approximately 18% of the patients had a history of cardiovascular disease. Moreover, 58% had history of hypertension, and 34% had a history of hyperlipidemia; 39% were current or former smokers.

Of the patients included in the study, 61.6% had a diagnosis of solid tumor, and 38.4% had a diagnosis of hematological malignancy. Approximately 5.8% of the patients with a solid tumor had metastatic disease at the time of inclusion in the study.

Of the total of 650 patients who were initially enrolled in the study, 46% were located in an intensive care unit (ICU) at the time of the code, and 55% were located on a regular medical floor. Approximately 60% of the patients had a code status discussion before cardiac resuscitation was performed, led by either the primary care or palliative care team.

We found that cardiopulmonary arrest was the most frequent precipitating cause in patients requiring CPR (44.6%). In more than 90% of the patients, the average chest compression rate, average compression depth, and overall number of compressions in the targeted zone were obtained, meeting all the required criteria for high-quality CPR.

The overall immediate survival rate (ROSC) was approximatively 80% after CPR efforts. Of the patients in whom ROSC was obtained, 59.1% were alive at 24 h. Heterogeneity in survival rates was observed in terms of cancer type. Successful resuscitation and survival at 24 h were obtained in 42.2% of patients with hematological tumors and in 57.8% patients with solid tumors. Resuscitation success rate for patients with metastatic disease was 9.5%.

Twenty percent of the patients who were on the regular medical floor and survived after CPR measures were admitted to the ICU post-CPR. Overall, 34.4% of patients who underwent CPR and survived changed their code status to DNR. Patients with hematological malignancies had the highest rate of post-CPR DNR status change (leukemia 40%, hematological stem cell transplantation recipients 30%, and lymphoma/myeloma 30%). This corresponds to

TABLE 1 Clinical Characteristics and Survival Rates of the 650 Patients Included in the Study

Age, yrs	
<50	174 (26.8)
>50	476 (73.2)
Sex	
Male	349 (53.7)
Female	301 (46.3)
Diagnosis	
Leukemia	128 (19.7)
Lymphoma/myeloma	64 (9.9)
Stem cell transplantation recipients	57 (8.8)
Breast cancer	43 (6.6)
Head and neck cancer	43 (6.6)
Gastrointestinal cancer	49 (7.5)
Thoracic cancer	67 (10.3)
Melanoma	13 (2.0)
Gynecological cancer	27 (4.2)
Urological cancer	22 (3.4)
Sarcoma	16 (2.5)
Colorectal cancer	11 (1.7)
Endocrine cancer	7 (1.0)
Genitourinary cancer	19 (2.9)
Other solid cancers	84 (12.9)
Metastatic cancer	38 (5.8)
Precipitating cause of CPR	
Cardiac arrest	290 (44.6)
Anaphylactic reaction	5 (0.8)
Respiratory failure	115 (17.7)
Arrhythmia	41 (6.3)
Hypovolemia	13 (2.0)
Other causes	62 (9.5)
No cause documented	124 (19.1)
Initial rhythm	
Pulseless electrical activity	171 (26.3)
Asystole	54 (8.3)
Bradycardia	52 (8.0)
Atrial fibrillation	3 (0.4)
Ventricular fibrillation	22 (3.4)
Ventricular tachycardia without pulse	15 (2.3)
Supraventricular tachycardia	13 (2.0)
Ventricular tachycardia with pulse	8 (1.2)
Other rhythm	39 (6.0)
No rhythm documented	273
Survival rate	
Immediate survival rate (ROSC)	520/650 80.0 (77.0–83.0)
Survival at 24 h	384/650 59.1 (55.3–62.9)

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TABLE 1 Continued

Survival at 24 h according to cancer type	
Hematological malignancy	162/384 (42.2)
Solid tumor	222/384 (57.8)
Metastatic solid tumor	21/222 (9.5)
Survival to discharge according to cancer type	
Overall survival to discharge	131/650 20.0 (16.9–23.1)
Hematological malignancy	46/650 (7.0)
Solid tumor	85/650 (13.0)
Code status change	
DNR code post-CPR	179/520 (34.4)

Values are n (%), n/N (95% confidence interval), or n/N (%).

CPR = cardiopulmonary resuscitation; DNR = do not resuscitate; ROSC = return of spontaneous circulation.

the low percentage of patients with hematological malignancies who underwent CPR and were discharged alive (7%). In patients with solid tumors, <30% changed their status to DNR post-CPR, whereas 13% were discharged alive. The median time from admission to DNR code status change was 26 days (interquartile range: 6 to 65 days); median time from cardiopulmonary arrest to DNR was 4 days (interquartile range: 2 to 5 days).

Although new technologies such as automated external defibrillators and changes in CPR guidelines have been introduced over the past decade, improvement in survival-to-hospital discharge in cancer patients after CPR is lacking. According to the American Society of Clinical Oncology 2019 Cancer Opinions Survey, about 66% of the U.S. adults who had or have cancer have thought about end-of-life care but only 20% have communicated their wishes to their physician (5). Improving the quality of end-of-life care requires a collaborative effort between cardiologists, oncologists, and palliative care services. There is a need to engage in honest discussions with cancer patients and their families using data concerning survival rates in cancer patients who underwent CPR. Published studies showed higher survival rates on survival to 30 days and survival to discharge rate for cancer patients, which is believed to be attributed to more changes in code status to DNR in patients with end-stage cancer (6). This change is also supported by the National Quality Forum and the American Society of Clinical Oncology, who recommend focusing on palliation and reducing the use of intensive medical services given the high costs and limited benefits of care in some types of cancer (7).

Several studies have stratified survival rates after CPR according to the type of cancer (hematological vs. solid), localized versus metastatic, and location at the time of cardiac arrest (2,8). Reisfield et al. (4) found that in 1,707 patients with solid tumors, the rate of discharge to home or other facility was 7.1% but was only 2% for patients with hematological malignancies. Consistent with these results, Hwang et al. (9) reported that in 41 patients with cancer who underwent out-of-hospital CPR, the rate of discharge to home was 4.9% overall but 18% for those with solid tumors compared with 12.5% for those with hematological malignancies. These results suggest that in patients with solid tumors, unexpected cardiac arrest may reflect reversible problems, and the patients may respond better to CPR. The survival rate of discharge to home for patients with metastatic cancer in our study (9.5%) is higher than most of the rates reported previously, which could be explained by the progress that has been made in the care of these patients and ICU management of patients who had cardiac arrest.

There are no clear objective guidelines toward the approach of changing code status in cancer patients. Our findings suggests that patients with hematological malignancies have a higher likelihood of changing their code status to DNR after surviving CPR. Larger randomized studies are needed to understand the independent contribution of cardiovascular risk factors in the outcomes of cancer patients undergoing CPR. A higher probability of DNR designation has been previously reported to be associated with male sex, the patient's awareness of the prognosis, the family's awareness of the patient's diagnosis and prognosis, and duration of ICU care >14 days (9). Better communication with patients and their families in these settings remains important.

A recently published meta-analysis of 11 randomized clinical trials found that CPR treatment discussions with patients led to a decrease in patients' CPR preference from 53.6% to 38.6% (risk ratio: 0.70; 95% confidence interval: 0.63 to 0.78) (10). The randomized trials selected patients with advanced diseases and a life expectancy <1 year, such as metastatic cancer, end-stage heart failure, and renal failure as inclusion criteria. The most effective communication intervention that helped to achieve these outcomes was the video-assisted decision aids. We believe, however, that this might lead to a more generic approach of the code status discussion and less of an individualized discussion that is required in cancer. The physician needs to tailor information for each patient and make an effort to understand the patient's values and preferences. Cancer patients need accurate, unbiased information about their condition and the risks and benefits of performing CPR. Adequate training for physicians to engage in end-of-life discussions is required to obtain

uniformity and consistency in the modality and timing of DNR decisions.

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