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Original Contribution

Long-term survival of out-of-hospital cardiac arrest patients with malignancy☆,☆☆

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ABSTRACT

Background: The aim of this study was to investigate whether the 1-year survival rate of out-of-hospital cardiac arrest (OHCA) patients with malignancy was different from that of those without malignancy.
Methods: All adult OHCA patients were retrospectively analyzed in a single institution for 6 years. The primary outcome was 1-year survival, and secondary outcomes were sustained return of spontaneous circulation (ROSC), survival to hospital admission, survival to discharge and discharge with a good neurological outcome (CPC 1 or 2). Kaplan-Meier survival analysis and Cox proportional hazard regression analysis were performed to test the effect of malignancy.
Results: Among 341 OHCA patients, 59 patients had malignancy (17.3%). Sustained ROSC, survival to admission, survival to discharge and discharge with a good CPC were not different between the two groups. The 1-year survival rate was lower in patients with malignancy (1.7% vs 11.4%; $P = 0.026$). Kaplan-Meier survival analysis revealed that patients with malignancy had a significantly lower 1-year survival rate when including all patients ($n = 341$; $P = 0.028$), patients with survival to admission ($n = 172$, $P = 0.002$), patients with discharge CPC 1 or 2 ($n = 18$, $P = 0.010$) and patients with discharge CPC 3 or 4 ($n = 57$, $P = 0.008$). Malignancy was an independent risk factor for 1-year mortality in the Cox proportional hazard regression analysis performed in patients with survival to admission and survival to discharge.
Conclusions: Although survival to admission, survival to discharge and discharge with a good CPC rate were not different, the 1-year survival rate was significantly lower in OHCA patients with malignancy than in those without malignancy.

1. Introduction

1.1. Background

Malignancy is the second leading cause of death among noncommunicable diseases and was responsible for 8.2 million deaths globally in 2012 [1]. In general, patients with advanced malignancy with metastasis or recurrence are subject to palliative care aimed at improving their quality of life. However, recent advances in cancer therapies, such as targeted chemotherapy, have led to longer lives for patients with malignancy, which is known to delay the patients' access to palliative care and the decision for advanced directives [2-5].

Complications related to malignancy itself or chemotherapy are common in this population. Consequently, acute care use and unexpected death have increased in patients with advanced malignancy [6]. Sudden cardiac arrest is one of the clinical presentations of unexpected death.

Overall survival to discharge rates from out-of-hospital cardiac arrest (OHCA) are approximately 10% [7,8]. However, there are little data about the prognosis of cardiac arrest in patients with malignancy. One meta-analysis including in-hospital cardiac arrest (IHCA) patients showed that the overall survival to hospital discharge in patients with cancer was comparable to that in unselected inpatients. A previous study included only IHCA cases, and long-term follow-up data were lacking [9]. Another study enrolled cancer patients who were admitted to the intensive care unit (ICU) after cardiac arrest [10]. The majority of enrolled cases were also IHCA cases, and the 6-month survival rate was not different from those in matched controls. A previous systematic review reported that the survival rates of patients with malignancy from cardiac arrest have improved over time and are increasingly comparable to those without malignancy [11]. To our knowledge, there is no

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study about the long-term outcome of OHCA patients with malignancy compared with those without malignancy.

1.2. Goal of this study

We hypothesized that the long-term survival rate of OHCA patients with malignancy would be lower than that of those without malignancy. To test this hypothesis, we compared the 1-year survival rates of OHCA patients with and without malignancy.

2. Methods

2.1. Study design and setting

This was a retrospective observational study that was performed in a single academic hospital emergency department (ED) with an annual census of approximately 70,000 patients.

Basic life support was administered by the fire station–based emergency medical technicians, and advanced life support was administered after transportation to the ED. If the patients were successfully resuscitated, the patients were admitted to the ICU for post-cardiac arrest care. Post-cardiac arrest care included hemodynamic optimization, therapeutic hypothermia at 33 °C for 24 h and emergent coronary angiography that was delivered at the discretion of the attending physician. Neurological outcome was evaluated using serial neurologic examinations, electroencephalography (EEG) and brain imaging. The withdrawal of active life-sustaining therapy was only allowed in brain-dead patients. If there was any electrical activity in the EEG or any brain stem function upon neurological examination, the discontinuation of active intensive care was not allowed in patients with persistent coma. Instead, the patients and their family could decide not to receive further life-sustaining treatment, such as renal replacement therapy, vasopressor use and additional cardiopulmonary resuscitation (CPR).

This study was approved by our institutional review board (IRB No. H-1608-067-784) and was exempt from patient informed consent.

2.2. Participants and data collection

We retrospectively identified all OHCA patients using a CPR registry in our electronic medical records system from January 1, 2009 to December 31, 2014. Patients younger than 18 years old and patients with traumatic causes of arrest, including hanging, intoxication and drowning, were excluded.

We collected data such as age, gender, witnessed cardiac arrest, bystander CPR, initial cardiac rhythm, any defibrillation, duration of CPR at ED, sustained return of spontaneous circulation (ROSC), survival to hospital admission, therapeutic hypothermia, survival to discharge, the discharge cerebral performance category (CPC) and 1-year survival. Discharge CPC 1 or 2 was considered a good neurological outcome. All data except 1-year survival were abstracted from both the CPR registry and the electronic medical records system by a research nurse who was blinded to the research design. For the validity of data, CPC status at discharge was re-evaluated by an independent physician. The agreement between the two CPC results was 99.7% (only one patient with CPC 4 in the CPR registry was determined to be CPC 3 by an independent physician). The Fleiss' Kappa value was 0.992 ($P < 0.001$), indicating an almost perfect inter-rater reliability. Mortality and the date of death were evaluated using the Korean Statistics database with a minimum follow-up duration of one year. Malignancy was defined as the presence of an active disease requiring therapeutic management, such as surgery, radiation or chemotherapy. Patients with no evidence of disease for 1 year were considered as not having an active malignancy. If the patient had a malignancy, then the type (solid tumor or hematologic malignancy) and anatomic site (solid tumor only) of the malignancy were further specified, and the presence of metastasis and recent chemotherapy (within 1 month) were evaluated.

2.3. Outcomes measures

Primary outcome was defined as a mortality of any cause at 1-year. Secondary outcome measures were sustained ROSC, survival to hospital admission, survival to discharge and survival to discharge with a good CPC.

2.4. Statistical analysis

Continuous variables were presented as the mean with 95% confidence intervals (CIs), and categorical variables were presented as the percent frequency of occurrence. Student's *t*-test or Wilcoxon rank-sum test was used to compare continuous variables, and the chi-square test or Fisher's exact test was used to compare categorical variables, as appropriate.

Kaplan-Meier survival analysis with log-rank test was used to compare the primary outcome. This test was also performed in the survival to hospital admission, discharge CPC 1 or 2 and discharge CPC 3 or 4 subgroups. Cox proportional hazard regression analysis for the prediction of 1-year mortality was performed to evaluate the independent effect of malignancy on the primary outcome. We have included variables that were significantly ($P < 0.10$) associated with 1-year mortality in the cox regression analysis (Supplement Table 1). Age, gender, witnessed cardiac arrest and malignancy were included in the model when this test was performed for all patients. Therapeutic hypothermia was added in the analysis performed for patients with survival to admission. Good neurological outcome was added in the analysis performed for patients with survival to discharge.

Two-tailed *P* values < 0.05 were considered to indicate statistical significance. All analyses were performed using Stata version 13.1 (Stata Corp, College Station, TX).

3. Results

3.1. Demographic characteristics

A total of 391 OHCA cases were identified during the 6-year study period. After excluding 50 cases with traumatic causes of arrest, 341 cases including 59 cases with malignancy (17.3%) were analyzed. Demographic characteristics were not different between the two groups (Table 1). No patients with malignancy had shockable rhythm at ED presentation, and defibrillation attempts were less frequently performed in patients with malignancy. The duration of CPR was significantly shorter in patients with malignancy, especially in whom ROSC was not achieved.

Overall survival to discharge, discharge with a good CPC and the 1-year survival rate was 22.0%, 5.3% and 9.7%, respectively. Sustained ROSC and the survival to admission rate were not different between the two groups. Therapeutic hypothermia was less frequently performed in patients with malignancy. Survival to discharge and discharge with a good CPC rates in patients with malignancy were lower than those without malignancy (18.6% vs 22.7%, 3.4% vs 5.7%). However, this difference was not statistically significant. The 1-year survival rate was significantly lower in patients with malignancy.

3.2. Characteristics of malignancy based on outcomes

Table 2 summarizes the characteristics of malignancy according to survival to admission and survival to discharge. The hepatobiliary pancreas and gastrointestinal tract (stomach and colon) were the most frequent anatomic sites for solid tumors. There was no significant difference among the types of malignancy regarding the survival to admission or survival to discharge rates. Two-thirds of the malignancy patients had metastasis, and one-third had received chemotherapy within 1 month. These characteristics were not associated with the survival to admission and survival to discharge rates.