The Potential Risk Factors for Mortality in Patients After In-Hospital Cardiac Arrest: A Multicenter Study

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Background and Purpose: In-hospital cardiac arrest (IHCA) has high mortality rate, which needs more research. This multi-center study aims to evaluate potential risk factors for mortality in patients after IHCA.

Methods: Data for this study retrospectively enrolled IHCA patients from 14 regional hospitals, two district hospitals, and five medical centers between 2013 June and 2018 December. The study enrolled 5,306 patients and there were 2,871 patients in subgroup of intensive care unit (ICU) and emergency room (ER), and 1,894 patients in subgroup of general wards.

Results: As for overall IHCA patients, odds ratio (OR) for mortality was higher in older patients (OR = 1.69; 95% CI:1.33–2.14), those treated with ventilator (OR = 1.79; 95% CI:1.36–2.38) and vasoactive agents (OR = 1.88; 95% CI:1.45–2.46). Whereas, better survival was reported in IHCA patients with initial rhythm as ventricular tachycardia (OR = 0.32; 95% CI: 0.21–0.50) and ventricular fibrillation (OR = 0.26; 95% CI: 0.16–0.42). With regard to ICU and ER subgroup, there was no mortality difference among different nursing shifts, whereas for patients in general wards, overnight shift (OR = 1.83; 95% CI: 1.07–3.11) leads to poor outcome.

Conclusion: For IHCA patients, old age, receiving ventilator support and vasoactive agents reported poor survival. Overnight shift had poor survival for IHCA patients in general wards, despite no significance in overall and ICU/ER subgroups.

Keywords: intensive care unit, in-hospital cardiac arrest, overnight shift, patient-to-nurse ratio, survival, targeted temperature management

INTRODUCTION

In-hospital cardiac arrest (IHCA) has high mortality rate (1). The majority of data are derived from the American Heart Association’s Get With The Guidelines-Resuscitation (GWTG-R) registry, which reported 9 to 10 IHCA cases per 1,000 admissions from 2008 to 2017 (2, 3).

Despite successful resuscitation, only few resuscitated patients have good neurologic conditions at discharge (4). Targeted temperature management (TTM) after cardiac arrest remains the primary neuroprotective approach following cardiac arrest (5, 6).
Compared to other critical cardiovascular conditions, including stroke, myocardial infarction, and OHCA, IHCA has received little attention (1). Thus, this study was conducted to evaluate the potential risk factors for mortality in patients after IHCA.

METHODS

This cross-sectional study analyzed the IHCA data set of The Taiwan Clinical Performance Indicator (TCPI) system, which was founded by the Joint Commission of Taiwan (JCT) in 2011. The Human Research Committee of Kaohsiung Veterans General Hospital approved this study.

Data Source and Study Population

This registered multicenter study retrospectively enrolled IHCA patients from 14 regional hospitals, two district hospitals, and five medical centers between June 2013 and December 2018. A total of 7,731 cases were included. We excluded patients with undetermined sex, age younger than 18 years, with a do-not-resuscitate (DNR) order, and those not receiving resuscitation. JCT staff supervised this registry and checked the numbers of IHCA patients to confirm that all IHCA patients in enrolled hospitals were included in this study. Finally, 5,306 patients were included in the analysis (Figure 1). The IHCA event locations were collected including intensive care unit (including coronary care units), emergent department, ordinary ward, examination room, postoperative recovery room, outpatient department, operating theater or coronary angiography laboratory and others. Total 54.1% of IHCA occurred in ICU/ER and 35.7% of IHCA occurred in general ward. Only 10.2% of IHCA occurred in examination room, postoperative recovery room, outpatient department, operating theater or coronary angiography laboratory, etc. Finally, there were 2,871 and 1,894

**FIGURE 1** | Flow-chart showing identification process of the study cohort.
### TABLE 1 | Basic characteristics of in-hospital cardiac arrest patients in a multicenter cohort study.

| Variables                                      | Total (N = 5,306) | Survival (N = 821) | Death (N = 4,485) | P-value  |
|------------------------------------------------|-------------------|--------------------|-------------------|----------|
| Sex                                            |                   |                    |                   |          |
| Male                                           | 3,335 (62.9%)     | 494 (60.2%)        | 2,841 (63.3%)     | 0.0836   |
| Female                                         | 1,971 (37.2%)     | 327 (39.8%)        | 1,644 (36.7%)     |          |
| Age                                            |                   |                    |                   |          |
| <70                                            | 2,537 (47.8%)     | 440 (53.6%)        | 2,097 (46.8%)     | 0.0003   |
| ≥70                                            | 2,769 (52.2%)     | 381 (46.4%)        | 2,388 (53.2%)     |          |
| Hospital level                                 |                   |                    |                   |          |
| Medical center                                 | 2,588 (48.8%)     | 309 (37.6%)        | 2,279 (50.8%)     | <0.0001  |
| Regional/district hospital                      | 2,718 (51.2%)     | 512 (62.4%)        | 2,206 (49.2 %)    |          |
| Hospital volume for admission                  |                   |                    |                   |          |
| (N = average people per month)                 |                   |                    |                   |          |
| <1,000                                         | 575 (10.8%)       | 79 (9.6%)          | 496 (11.1%)       |          |
| 1,000 ≤ N < 2,000                             | 1,070 (20.2%)     | 196 (23.9%)        | 874 (19.5%)       |          |
| 2,000 ≤ N < 3,000                             | 1,027 (19.4%)     | 219 (26.7%)        | 808 (18.0%)       |          |
| N ≥ 3,000                                      | 2,634 (49.6%)     | 327 (39.8%)        | 2,307 (51.4%)     |          |
| Hospital volume for emergency department       |                   |                    |                   |          |
| (N = average people per month)                 |                   |                    |                   |          |
| <3,000                                         | 324 (6.1%)        | 33 (4.0%)          | 291 (6.5%)        | <0.0001  |
| 3,000 ≤ N < 5,000                             | 1,771 (33.4%)     | 335 (40.6%)        | 1,436 (32.0%)     |          |
| 5,000 ≤ N < 7,000                             | 1,454 (27.4%)     | 282 (34.4%)        | 1,172 (26.1%)     |          |
| N ≥ 7,000                                      | 1,757 (33.1%)     | 171 (20.8%)        | 1,586 (35.4%)     |          |
| Total beds per hospital                        |                   |                    |                   |          |
| <500                                           | 974 (18.4%)       | 145 (17.7%)        | 829 (18.5%)       | 0.0024   |
| 500–1,000                                      | 1,600 (30.2%)     | 289 (35.2%)        | 1,311 (29.2%)     |          |
| ≥1,000                                         | 2,732 (51.5%)     | 387 (47.1%)        | 2,345 (52.3%)     |          |
| Event time                                     | 3,456 (65.1%)     | 459 (55.9%)        | 2,997 (66.8%)     | <0.0001  |
| Years                                          | 1,850 (34.9%)     | 362 (44.1%)        | 1,488 (33.2%)     |          |
| Months                                         |                   |                    |                   |          |
| March to May                                   | 1,334 (25.1%)     | 220 (26.8%)        | 1,114 (24.8%)     | 0.5994   |
| June to August                                 | 1,216 (22.9%)     | 177 (21.6%)        | 1,039 (23.2%)     |          |
| September to November                          | 1,247 (23.5%)     | 193 (23.5%)        | 1,054 (23.5%)     |          |
| Office hour                                    |                   |                    |                   |          |
| Office hour                                    | 3,384 (63.9%)     | 547 (66.6%)        | 2,837 (63.3%)     | 0.0647   |
| Non-office hour                                | 1,922 (36.2%)     | 274 (33.4%)        | 1,648 (36.7%)     |          |
| Shift                                          |                   |                    |                   |          |
| 08:00–16:00                                    | 1,913 (36.1%)     | 337 (41.1%)        | 1,576 (35.1%)     | <0.0001  |
| 16:00–24:00                                    | 1,489 (28.1%)     | 274 (33.4%)        | 1,215 (27.1%)     |          |
| 24:00–08:00                                    | 1,904 (35.9%)     | 210 (25.6%)        | 1,694 (37.8%)     |          |
| Event location                                 | 1,866 (35.2%)     | 257 (31.3%)        | 1,609 (35.9%)     | <0.0001  |
| Intensive care unit                            | 360 (6.8%)        | 89 (10.6%)         | 271 (6.0%)        |          |
| Examination room                               | 1,005 (18.9%)     | 170 (20.7%)        | 835 (18.6%)       |          |
| Emergent department                            | 1,894 (35.7%)     | 273 (33.3%)        | 1,621 (36.1%)     |          |
| Ordinary ward                                  | 181 (3.4%)        | 32 (3.9%)          | 149 (3.3%)        |          |
| Witness                                        |                   |                    |                   |          |
| With                                           | 4,560 (85.9%)     | 781 (95.1%)        | 3,779 (84.3%)     | <0.0001  |
| With treatment/procedure before ALS            | 4,194 (79.0%)     | 694 (84.5%)        | 3,500 (78.0%)     | <0.0001  |
| Intravascular catheter                         | 3,816 (71.9%)     | 640 (78.0%)        | 3,176 (70.8%)     | <0.0001  |
| Intravascular medication                       | 2,932 (55.3%)     | 455 (54.4%)        | 2,477 (55.2%)     | 0.9191   |
| Electrocardiogram monitor                      | 2,708 (51.0%)     | 448 (54.6%)        | 2,260 (50.4%)     | 0.0277   |
| Intubation                                      | 1,615 (30.4%)     | 213 (25.9%)        | 1,402 (31.3%)     | 0.0023   |
| Ventilator                                      | 1,513 (28.5%)     | 200 (24.4%)        | 1,313 (29.3%)     | 0.0041   |
| Intracardiac pacemaker or defibrillator        | 105 (2.0%)        | 19 (2.3%)          | 86 (1.9%)         | 0.4530   |
| Arterial line                                   | 747 (14.1%)       | 109 (13.3%)        | 638 (14.2%)       | 0.4724   |
| Cause of IHCA                                   |                   |                    |                   |          |
| Fatal arrhythm                                 | 1,893 (35.7%)     | 366 (44.6%)        | 1,527 (34.1%)     | <0.0001  |
| Hypotension                                     | 658 (12.4%)       | 56 (6.8%)          | 602 (13.4%)       |          |
| Respiratory depression                         | 792 (14.9%)       | 118 (14.4%)        | 674 (15.0%)       |          |

(Continued)
### Table 1: Continued

| Variables                          | Total \(N = 5,306\) | Survival \(N = 821\) | Death \(N = 4,485\) | \(P\)-value |
|------------------------------------|----------------------|----------------------|----------------------|-------------|
| Metabolism                         | 180 (3.4%)           | 21 (2.6%)            | 159 (3.6%)           |             |
| Myocardial ischemia/infarction     | 389 (7.3%)           | 55 (6.7%)            | 334 (7.5%)           |             |
| Others                             | 1,394 (26.3%)        | 205 (25.0%)          | 1,189 (26.5%)        |             |
| **ALS item**                       |                      |                      |                      |             |
| Chest compression                  | 4,696 (88.5%)        | 727 (88.6%)          | 3,969 (88.5%)        | 0.9634      |
| Electrical discharge               | 1,118 (21.1%)        | 309 (37.6%)          | 809 (18.0%)          | <0.0001     |
| Airway management                  | 3,422 (64.5%)        | 543 (66.1%)          | 2,879 (64.2%)        | 0.2838      |
| Vasoactive agents                  | 4,132 (77.9%)        | 579 (70.5%)          | 3,553 (79.2%)        | <0.0001     |
| **Vital sign before ALS**          |                      |                      |                      |             |
| Conscious                          | With 597 (11.3%)     | 102 (12.4%)          | 495 (11.0%)          | 0.3430      |
|                                    | Without 4,377 (82.5%)| 674 (82.1%)          | 3,703 (82.6%)        |             |
| Respiration                        | With 1,564 (29.5%)   | 250 (30.5%)          | 1,314 (29.3%)        | 0.4768      |
|                                    | Without 3,834 (63.8%)| 523 (63.7%)          | 2,861 (63.8%)        |             |
| Pulse                              | Present 1,382 (26.1%)| 226 (27.5%)          | 1,156 (25.8%)        | 0.5364      |
|                                    | Absent 3,565 (67.2%)  | 543 (66.1%)          | 3,022 (67.4%)        |             |
| **Initial rhythm**                 |                      |                      |                      |             |
| Ventricular fibrillation           | 276 (5.2%)           | 94 (11.5%)           | 182 (4.1%)           | <0.0001     |
| Ventricular tachycardia            | 548 (10.3%)          | 179 (21.8%)          | 369 (8.2%)           |             |
| Asystole                           | 1,457 (27.5%)        | 155 (18.9%)          | 1,302 (29.1%)        |             |
| Pulseless electrical activity      | 2,205 (41.6%)        | 267 (32.5%)          | 1,938 (43.2%)        |             |
| Bradycardia                        | 717 (13.5%)          | 102 (12.4%)          | 615 (13.7%)          |             |
| Perfuising rhythm                  | 94 (1.8%)            | 22 (2.7%)            | 72 (1.6%)            |             |
| **Start in-hospital resuscitation teams** | Yes 2,148 (67.9%)   | 392 (67.6%)          | 1,756 (67.9%)        | 0.8822      |
| **Reason of CPR termination**      |                      |                      |                      |             |
| Death                              | 1,378 (26.0%)        | 0 (0.0%)             | 1,378 (30.7%)        | <0.0001     |
| Medical futility                  | 498 (9.4%)           | 13 (1.6%)            | 485 (10.8%)          |             |
| DNR                                | 949 (17.9%)          | 15 (1.8%)            | 934 (20.8%)          |             |
| ROSC                               | 2,447 (46.1%)        | 787 (95.9%)          | 1,660 (37.0%)        |             |
| Mechanical support (ECMO)          | 34 (0.6%)            | 6 (0.7%)             | 28 (0.6%)            |             |
| **Targeted temperature management**|                      |                      |                      |             |
| With                               | 24 (0.5%)            | 9 (1.1%)             | 15 (0.3%)            | 0.0028      |

**Note:** ALS, advanced life support; CPR, cardiopulmonary resuscitation; DNR, do-not-resuscitate; ECMO, Extracorporeal Membrane Oxygenation; IHCA, in-hospital cardiac arrest; ROSC, Return of spontaneous circulation.

Statistical Analysis

For data analysis, SAS software version 9.4 (SAS Institute, Inc., Cary, NC) was used. Percentile values were used to express categorical data, analyzed using the chi-square test. Multivariable logistic regression model was used to calculate odds ratio (OR) and associated 95% confidence intervals (95% CIs) for significant variables, including sex, age, hospital level, direct cause, and initial rhythm. A \(P\)-value <0.05 was considered statistically significant.

**RESULTS**

The patients’ basic characteristics are listed in Table 1. The majority of the initially detected rhythms were pulseless electrical...
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**FIGURE 2** Comparisons of survival rate of individual clinical characteristic of in-hospital-cardiac-arrest (IHCA) patients. (A) There was no sex difference in survival (male: 14.8%; female: 16.6%, \( P = 0.0836 \)). (B–F) Factors for poor survival included old age (<70 years: 17.3%; \( \geq 70 \) years: 13.8%, \( P = 0.0003 \)), medical center (medical center: 11.9%; regional/district hospital: 18.8%, \( P < 0.0001 \)), large hospital volume for admission with >3,000 patients per month on average, large hospital volume for emergency room with >7,000 patients per month on average, and total beds >1,000. (G) Events occurring in the recent year had better outcomes. (H) There was no difference in IHCA outcome among different months. (I) There was no difference in IHCA outcome between events occurring during office and non-office hours. (J) Events occurring between 24:00 and 08:00 showed poor outcomes. (K) Event location at intensive care unit (ICU) showed poor outcomes, whereas, event location at examination room presented better outcomes (ICU: 13.8%; examination room: 24.7%; emergent department: 16.9%; ordinary ward: 14.4%; others: 17.7%, \( P < 0.0001 \)). (L) Better survival was reported in patients with a witness (with: 17.1% without: 5.6%, \( P < 0.0001 \)).

Survival ratios of IHCA patients according to basic characteristics are shown in Figure 2. There was no sex difference in survival ratios (Figure 2A). Factors for poor survival included old age (Figure 2B), medical center (Figure 2C), large hospital volume for admission with >3,000 patients per month on average (Figure 2D), and total beds >1,000 (Figure 2F). Events occurring between 24:00 and 08:00 had poor outcomes (Figure 2J). Events occurring at the ICU showed poor outcomes, whereas events at the examination room showed better outcomes (Figure 2K). Moreover, better survival was reported in patients with a witness during the attack (Figure 2L).

Figure 3 includes survival ratios of treatment or procedure before ALS and ALS-associated items. The survival ratio with different causes of IHCA and other managements are reported in Figure 4. Fatal arrhythmia as the cause of IHCA had better survival (Figure 4A). Patients who underwent TTM had better outcomes (Figure 4B). Initially-detected ventricular fibrillation (VF) was associated with better survival ratios (Figure 4D). Moreover, there was no difference in survival between patients with and without in-hospital resuscitation teams (Figure 4C).

The basic characteristics of the general ward and ICU/ER subgroups are reported in Table 2. The general ward subgroup had more patients aged >70 years and more IHCA events occurring during overnight shifts. The ICU/ER subgroup had more IHCA events occurring during office hours, more witnessed IHCA patients, and more patients receiving treatment or procedure before ALS. Moreover, the proportion of starting in-hospital resuscitation teams was higher in the general subgroup.

In the multivariable logistic regression model, OR for mortality was higher in older patients, those receiving ventilator support before ALS, and those receiving vasoactive agents during ALS in the overall IHCA patient group (Table 3). On the contrary, patients with respiratory depression as the cause of IHCA, rather than hypotension showed better outcomes. In the ICU/ER subgroup (Table 3), better survival was reported in patients with respiratory depression rather than hypotension as the cause of IHCA, and patients with initially detected VT and VF had better outcome. For the general ward subgroup, patients with older age and attacks occurring between 24:00 and 08:00...
Old Age Is a Predictor of Worse Overall Outcome

Age is one of the predictors of the Cardiac Arrest Survival Post Resuscitation In-hospital Score (CASPRI) score. A previous study indicated that increased age is associated with poor survival, especially for patients aged >70 years (1, 14). One single-center analysis of IHCA outcomes indicated that younger patients were more likely to survive the initial IHCA (15), which supported our study finding that age ≥70 years (OR = 1.69; 95% CI: 1.33–2.14) (Table 3) was a predictor of worse overall outcome.

Overnight Shift in General Wards Increased Mortality Risk of IHCA Patients

The patient-to-nurse ratio should be <9:1 in medical centers, 1:2:1 in regional hospitals, and 15:1 in district hospitals, according to Taiwan’s local medical law standards. However, in Taiwan, the actual patient-to-nurse ratio is approximately 10–11:1 in general wards for day shifts and 20–30:1 for night shifts. This workload (compared to 08:00–17:00) had poor outcomes. Moreover, initial rhythms of VT and VF were shown to reduce the mortality risk in IHCA patients in overall, ICU/ER and general ward subgroups.

DISCUSSION

This multicenter cohort study analyzed the association between IHCA patients and healthcare-related risk factors. Compared to the previous GWTG-R cohort data from the United States (U.S.) involving IHCA patients with a mean age of 66 years, our patients’ mean age was 68 years and 62.9% of our patients were male (Table 1), whereas in the GWTG-R, 58% were male. The presenting rhythm in the GWTG-R was most often non-shockable (81%), which was comparable to our study finding that 82.6% of the patients had a non-shockable rhythm (1, 2). Survival to hospital discharge was ~25% in GWTG-R, whereas in our study, this was 15.5% (2). Previous study had a 7-year follow-up between 2000 and 2004 (12). Moreover, advanced cardiac life support (ACLS) training and adherence contributed to better outcome of IHCA patients (13). Whereas, in comparison to previous study (11), rate of survival to discharge in overnight shift was not improved (14.7 vs. 11.03%), which might be attributed to hospital level and disease severity.
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FIGURE 4 | Comparisons of survival rate of different causes and initial rhythm of in-hospital-cardiac-arrest (IHCA) and other specific managements. (A) Fatal arrhythmia as the cause of IHCA had better survival. (B) Patients who underwent TTM (with: 37.5%; without TTM: 15.4%, \( P = 0.0028 \)) had better outcomes. (C) Starting in-hospital resuscitation teams had no benefit on survival (with: 18.3%; without: 18.5%, \( P = 0.8822 \)). (D) Initially detected ventricular fibrillation (VF) revealed better survival rates (VF: 34.1%; ventricular tachycardia (VT): 32.7%; asystole: 10.6%; PEA: 12.1%; bradycardia: 14.2%; perfusing rhythm: 23.4%; unknown: 22.2%, \( P < 0.0001 \)).
### TABLE 2 | Basic characteristics of in-hospital cardiac arrest patients in subgroups of general wards and intensive care unit/emergency room.

| Variables | General wards | ICU/ER | P-value |
|-----------|---------------|--------|---------|
|           | (N = 1,894)   | (N = 2,871) |         |
| Sex       |               |         |         |
| Male      | 1,181 (62.4%) | 1,847 (64.3%) | 0.1650 |
| Female    | 713 (37.7%)   | 1,024 (35.7%) |         |
| Age <70   | 797 (42.1%)   | 1,480 (51.6%) | <0.0001 |
| ≥70       | 1,097 (57.9%) | 1,391 (48.5%) |         |
| Hospital level |         |         |         |
| Medical center | 904 (47.7%) | 1,509 (52.6%) | 0.0025 |
| Regional/district hospital | 990 (52.3%) | 1,362 (47.4%) |         |
| Hospital volume for admission (N = average people per month) | | | <0.0001 |
| N < 1,000 | 176 (9.3%)   | 377 (13.1%)   |         |
| 1,000 ≤ N < 2,000 | 359 (19.0%) | 621 (21.6%)   |         |
| 2,000 ≤ N < 3,000 | 401 (21.2%) | 381 (13.3%)   |         |
| N ≥ 3,000 | 958 (50.6%)  | 1,492 (52.0%) |         |
| Hospital volume for emergency department (N = average people per month) | | | 0.1466 |
| N < 3,000 | 217 (11.5%)  | 398 (13.9%)   |         |
| 3,000 ≤ N < 5,000 | 531 (28.0%) | 799 (27.8%)   |         |
| 5,000 ≤ N < 7,000 | 498 (26.3%) | 704 (24.5%)   |         |
| N ≥ 7,000 | 648 (34.2%)  | 979 (34.1%)   |         |
| Total beds per hospital | | | <0.0001 |
| <500      | 266 (14.0%)  | 666 (23.2%)   |         |
| 500–1,000 | 723 (38.2%)  | 730 (25.4%)   |         |
| ≥1,000    | 905 (47.8%)  | 1,475 (51.4%) |         |
| Event time |           |        |         |
| Years     |               |         |         |
| 2013–2016 | 1,187 (62.7%) | 1,891 (65.9%) | 0.0241 |
| 2017–2018 | 707 (37.3%)  | 980 (34.1%)  |         |
| Months    |               |         |         |
| March to May | 461 (24.3%) | 723 (25.2%)   |         |
| June to August | 468 (24.7%) | 637 (22.2%)   |         |
| September to November | 421 (22.2%) | 699 (24.4%)   |         |
| December to February | 544 (28.7%) | 812 (28.3%)   |         |
| Office hour |           |        |         |
| Office hour | 1,118 (59.0%) | 1,897 (66.1%) | <0.0001 |
| Non office hour | 776 (41.0%) | 980 (33.9%)   |         |
| Shift     |               |         |         |
| 08:00–16:00 | 601 (31.7%) | 1,046 (36.4%) | <0.0001 |
| 16:00–24:00 | 501 (26.5%) | 848 (29.5%)   |         |
| 24:00–08:00 | 792 (41.8%) | 977 (34.0%)   |         |
| Witness   |               |         |         |
| With      | 1,569 (82.8%) | 2,511 (87.5%) | <0.0001 |
| Without treatment/ procedure before ALS | 1,454 (76.8%) | 2,318 (80.7%) | 0.0010 |
| Intravascular catheter | 1,314 (69.4%) | 2,139 (74.5%) | 0.0001 |
| Intravascular medication | 828 (43.7%) | 1,835 (63.9%) | <0.0001 |
| Electrocardiogram monitor | 430 (22.7%) | 1,985 (69.1%) | <0.0001 |
| Intubation | 129 (6.8%) | 1,324 (46.1%) | <0.0001 |
| Ventilator | 117 (6.2%) | 1,248 (43.5%) | <0.0001 |
| Intracardiac pacemaker or defibrillator | 12 (0.6%) | 75 (2.6%) | <0.0001 |
| Arterial line | 19 (1.0%) | 643 (22.4%) | <0.0001 |
| Cause of IHCA | | | <0.0001 |
| Fatal arrhythmia | 528 (27.9%) | 1,214 (42.3%) | <0.0001 |
| Hypotension | 152 (8.0%) | 446 (15.5%) |         |
| Respiratory depression | 451 (23.8%) | 286 (10.0%) |         |
| Metabolism | 49 (2.6%) | 113 (3.9%) |         |
| Myocardial ischemia/infarction | 104 (5.5%) | 205 (7.1%) |         |
| Others | 610 (32.2%) | 607 (21.1%) |         |
| ALS item |            |        |         |
| Chest compression | 1,678 (88.6%) | 2,523 (87.9%) | 0.4535 |

(Continued)
TABLE 2 | Continued

| Variables                        | General wards (N = 1,894) | ICU/ER (N = 2,871) | P-value |
|----------------------------------|---------------------------|-------------------|---------|
| Electrical discharge             | 304 (16.1%)               | 658 (22.9%)       | <0.0001 |
| Airway management                | 1,490 (78.7%)             | 1,576 (54.9%)     | <0.0001 |
| Vasoactive agents                | 1,384 (73.1%)             | 2,338 (81.4%)     | <0.0001 |
| Vital sign before ALS            |                           |                   |         |
| Conscious                        | With 187 (9.9%)           | 338 (11.8%)       | 0.0002  |
|                                 | Without 1,615 (85.3%)     | 2,325 (81.0%)     |         |
| Respiration                      | With 415 (21.9%)          | 990 (34.5%)       | <0.0001 |
|                                 | Without 1,377 (72.7%)     | 1,659 (57.8%)     |         |
| Pulse                            | Present 429 (22.7%)       | 806 (28.1%)       | <0.0001 |
|                                 | Absent 1,361 (71.9%)      | 1,847 (64.3%)     |         |
| Initial rhythm                   |                           |                   |         |
| Ventricular fibrillation         | 72 (3.8%)                 | 171 (6.0%)        | <0.0001 |
| Ventricular tachycardia          | 109 (5.8%)                | 366 (12.8%)       |         |
| Asystole                         | 794 (41.9%)               | 514 (17.9%)       |         |
| Pulseless electrical activity    | 706 (37.3%)               | 1293 (45.0%)      |         |
| Bradycardia                      | 165 (8.7%)                | 489 (17.0%)       |         |
| Perfusing rhythm                 | 48 (2.5%)                 | 38 (1.3%)         |         |
| Start in-hospital resuscitation teams | 1,051 (55.5%)         | 863 (30.1%)       | <0.0001 |
| Reason of CPR termination        |                           |                   |         |
| Death                            | 479 (25.3%)               | 751 (26.2%)       | 0.0016  |
| Medical futility                 | 164 (8.7%)                | 289 (10.1%)       |         |
| DNR                              | 386 (20.4%)               | 504 (17.6%)       |         |
| ROSC                             | 863 (45.6%)               | 1,305 (45.5%)     |         |
| Mechanical support               | 2 (0.1%)                  | 22 (0.8%)         |         |
| Targeted temperature management  | 7 (0.37%)                 | 12 (0.42%)        | 0.7954  |

ALS, advanced life support; CPR, cardiopulmonary resuscitation; DNR, do not resuscitate; IHCA, in-hospital cardiac arrest; ROSC, Return of spontaneous circulation.

is five times higher than that of institutions in Europe or the U.S (16, 17).

Previous research reported 31% mortality for a 8:1 ratio for patients within 30 days of hospitalization (18, 19). Our study reported that overnight shift was associated with increased mortality of IHCA patients in general wards, which could be attributed to the highly disproportionate patient-to-nurse ratios and overload for overnight nursing staff in general wards (20). Previous study with a large sample size with 86,748 IHCA patients (58, 593 cases during day/evening hours; 28,155 cases during night hours) indicated lower survival during night hours in comparison with event occurred during day/evening hours (11), which supported our result.

Initially-Detected VT/VF and Respiratory Depression as the Direct Cause of IHCA had Better Survival

Compared to all rhythms and non-shockable rhythms, VF and pulseless VT showed better survival and were two to three times more likely to survive to hospital discharge (1, 21). Higher prevalence of respiratory insufficiency was shown if the duration of preceding hospitalization was longer (22). Pre-existing data indicated that attempts at intubation may delay timely defibrillation and interruption in chest compressions, contributing to poor outcomes (23). However, in patients with respiratory depression as the cause of IHCA, intubation was not associated with worse survival (24).

Our study reported that patients with respiratory depression as the cause of IHCA had better survival in overall cohort and ICU/ER subgroup, but not in general ward subgroup. This result might be due to the fact that predictable or avoidable cardiac arrest may occur if patients had respiratory depression as the direct cause of IHCA events, and whether timely intubation affect survival.

IHCA Patients With a Witness Showed Better Survival, and No Survival Difference Was Noted Between Patients With and Without In-Hospital Resuscitation Teams

Many IHCA cases are considered preventable or avoidable, and witnessed IHCA events are associated with improved outcomes (25, 26). Our study reported that witnessed IHCA patients in the ICU/ER subgroup did not have better outcomes, whereas the overall cohort and general ward subgroup showed better outcomes. This difference could be attributed to the existence of well-monitored settings and alarm systems in
TABLE 3 | Multivariable logistic regression model on survival of IHCA patients. (N = 5,306).

| Variables                          | Overall (N = 5,306) | ICU and ER (N = 2,871) | General Ward (N = 1,894) |
|------------------------------------|---------------------|------------------------|--------------------------|
|                                    | Adjusted OR (95% CI) | P-value                | Adjusted OR (95% CI)     | P-value    | Adjusted OR (95% CI) | P-value    |
| Male                               | 1.26 (1.00–1.60)    | 0.0525                 | 1.40 (1.01–1.95)         | 0.0456     | 1.18 (0.78–1.81)     | 0.4335     |
| Age ≥70                            | 1.69 (1.33–2.14)    | <0.0001                | 1.48 (1.07–2.06)         | 0.0196     | 2.24 (1.47–3.42)     | 0.0002     |
| Hospital level-Medical center      | 1.53 (1.12–2.08)    | 0.0072                 | 1.57 (1.02–2.43)         | 0.0412     | 1.27 (0.71–2.26)     | 0.4238     |
| Non-office hour                    | 1.27 (0.99–1.61)    | 0.0668                 | 1.15 (0.82–1.62)         | 0.4083     | 1.27 (0.82–1.96)     | 0.2847     |
| Shift (Reference: 08:00–17:00)     |                     |                        |                          |            |                        |            |
| 24:00–08:00                        | 1.24 (0.92–1.66)    | 0.1585                 | 0.59 (0.32–1.10)         | 0.0966     | 1.83 (1.07–3.11)     | 0.0268     |
| 17:00–24:00                        | 0.81 (0.62–1.06)    | 0.1210                 | 0.67 (0.40–1.12)         | 0.1263     | 0.97 (0.60–1.58)     | 0.9028     |
| With witness                       | 0.43 (0.16–1.11)    | 0.0803                 | 1.02 (0.10–11.06)        | 0.9849     | 0.47 (0.16–1.41)     | 0.1783     |
| Treatment/procedure before ALS     |                     |                        |                          |            |                        |            |
| Intravascular catheter             | 0.93 (0.67–1.30)    | 0.6763                 | 0.65 (0.38–1.12)         | 0.1223     | 1.14 (0.64–2.04)     | 0.6604     |
| Intravascular medication           | 1.31 (1.00–1.70)    | 0.0463                 | 1.72 (1.18–2.52)         | 0.0047     | 1.07 (0.67–1.69)     | 0.7826     |
| Ventilator                         | 1.79 (1.36–2.38)    | <0.0001                | 1.95 (1.36–2.79)         | 0.0003     | 1.03 (0.43–2.50)     | 0.9467     |
| Intracardiac pacemaker or defibrillator | 1.99 (0.94–4.19) | 0.0706                | 1.97 (0.80–4.87)         | 0.1403     | 0.74 (0.07–8.12)     | 0.8055     |
| Cause (Reference: Hypotension)     |                     |                        |                          |            |                        |            |
| Myocardial ischemia/infarction     | 0.91 (0.56–1.47)    | 0.6945                 | 0.68 (0.33–1.40)         | 0.2994     | 1.44 (0.52–3.97)     | 0.4798     |
| Metabolism                         | 0.69 (0.39–1.23)    | 0.2070                 | 0.39 (0.18–0.83)         | 0.0149     | 1.01 (0.30–3.40)     | 0.9846     |
| Respiratory depression             | 0.59 (0.40–0.87)    | 0.0071                 | 0.37 (0.21–0.67)         | 0.0010     | 0.72 (0.37–1.42)     | 0.3418     |
| Fatal arrhythmia                   | 0.56 (0.39–0.82)    | 0.0026                 | 0.39 (0.23–0.67)         | 0.0005     | 0.56 (0.27–1.16)     | 0.1195     |
| ALS order                          |                     |                        |                          |            |                        |            |
| Chest compression                  | 1.06 (0.73–1.54)    | 0.7652                 | 1.24 (0.75–2.04)         | 0.3991     | 1.51 (0.70–3.24)     | 0.2921     |
| Electrical discharge               | 0.88 (0.64–1.20)    | 0.4002                 | 0.87 (0.56–1.34)         | 0.5240     | 1.08 (0.61–1.92)     | 0.7988     |
| Airway management                  | 0.96 (0.74–1.26)    | 0.7883                 | 0.92 (0.64–1.34)         | 0.6753     | 0.90 (0.53–1.54)     | 0.7064     |
| Vasoactive agents                 | 1.86 (1.45–2.36)    | <0.0001                | 1.77 (1.22–2.59)         | 0.0030     | 1.74 (1.07–2.83)     | 0.0250     |
| With Respiration                   | 0.93 (0.72–1.22)    | 0.6086                 | 0.88 (0.61–1.27)         | 0.5027     | 0.93 (0.55–1.58)     | 0.7989     |
| Initial rhythm (Reference: Asystole) |                     |                        |                          |            |                        |            |
| Perfusing rhythm                   | 0.71 (0.32–1.55)    | 0.3879                 | 0.46 (0.12–1.79)         | 0.2597     | 1.10 (0.35–3.47)     | 0.8652     |
| Bradycardia                        | 0.62 (0.42–0.91)    | 0.0156                 | 0.70 (0.39–1.27)         | 0.2417     | 0.63 (0.32–1.26)     | 0.1923     |
| PEA                                | 0.79 (0.56–1.12)    | 0.1811                 | 0.84 (0.48–1.46)         | 0.5302     | 0.84 (0.49–1.45)     | 0.5393     |
| Ventricular Tachycardia            | 0.32 (0.21–0.50)    | <0.0001                | 0.32 (0.16–0.62)         | 0.0007     | 0.28 (0.12–0.67)     | 0.0044     |
| Ventricular Fibrillation           | 0.26 (0.16–0.42)    | <0.0001                | 0.24 (0.11–0.51)         | 0.0002     | 0.34 (0.15–0.81)     | 0.0149     |
| Start in-hospital resuscitation teams | 1.21 (0.93–1.56) | 0.1512                | 1.27 (0.90–1.81)         | 0.1781     | 0.59 (0.27–1.28)     | 0.1781     |

ICU/ER to offer timely response, despite the absence of a witness.

Early detected cardiac arrest events in monitored settings and early warning systems are associated with improved outcomes (27, 28). Event location at an examination room showed better outcomes in our study (Figure 2K). In our study, there was no survival difference between patients with and without in-hospital resuscitation teams (Figure 4C) (Table 3). This result is the contribution of well-trained staff, with sufficient skills to respond to possible preventable IHCA events in usual care.

Study Limitations

First, our data were acquired from a unified medical record sheet filled out by professional practitioners, and information on comorbidities, past medical history, and underlying diseases were unavailable. Thus, post-resuscitation survival predictor such as CASPRI score could not be calculated. Second, detailed information such as definite collapse time, vital sign before resuscitation, and initial rhythm at collapse were not shown if IHCA events occurred in situations without monitor or witness. Moreover, resuscitation time, other interventions or devices and additional medical therapy were not documented. Finally, this was a multicenter, registered study, thus, future prospective randomized studies are required to confirm our findings. Finally, patients who underwent TTM had better outcomes, and this result was associated with the impact of TTM on post-resuscitation development rather than selection bias. However, this study enrolled IHCA patients between 2013 June and 2018 December, whereas national health insurance in Taiwan did not covered TTM until 2018 June. Selection bias might exist once life expectancy and economic issue were considered, however, there was no difference in terms of proportion of hypotension as cause of IHCA regardless receiving TTM or...
not (with: 16.67%; without: 12.38%, \( P = 0.5293 \)). Furthermore, compared with previous study more than one decade ago, despite the improvement in ACLS training, rate of survival to discharge in overnight shift was not improved, which might be attributed to hospital level and disease severity. However, the evaluation of disease severity was our limitation.

**Study Strengths**

This large registered multicenter study for adult IHCA patients enrolled different hospital levels and evaluated potential risk factors for mortality in patients after IHCA. Previous large sample size study focused on the association between survival and event time, thus it divided IHCA patients into events occurred during night hours and during day/evening hours (1). Our study analyzed the differences between survival and death subgroups to get information about the potential risk factors for IHCA mortality. Moreover, comparison between general wards and ICU/ER subgroups also strengthened the impact of patient-to-nurse ratios on survival for IHCA patients. The finding that overnight shift increased the mortality risk of IHCA patients in general wards or in both ICU and ER prompts the effort to achieve better work environments and decrease patient-to-nurse ratios in the future.

**CONCLUSIONS**

IHCA patients, including those in ICUs, ERs, and general wards, who are receiving ventilator support and vasoactive agents had poor survival. Better survival was observed in patients with VT and VF as initial rhythms. However, old age had a negative effect on overall survival. Overnight shifts were associated with poor survival in the general ward subgroup, although no significance was found in the overall cohort and ICU/ER subgroup. Thus, efforts to decrease patient-to-nurse ratios during overnights shift might improve survival in patients after IHCA.

**DATA AVAILABILITY STATEMENT**

The original contributions generated for this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

**ETHICS STATEMENT**

The studies involving human participants were reviewed and approved by The Institutional Review Board (IRB) of the Kaohsiung Veterans General Hospital approved this study (No. VGHKS19- EM 12-01). Written informed consent was not required for this study as the ICT dataset consists of de-identified secondary data for research purposes. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

**AUTHOR CONTRIBUTIONS**

W-CH: concept and design. S-YW and E-HY: acquisition, analysis, or interpretation of data. M-TW: drafting of the manuscript. W-CH and DY: critical revision of the manuscript for important intellectual content. S-YW and E-HY: statistical analysis. W-CH: administrative, technical, or material support. W-CH and H-HL: supervision. All authors contributed to the article and approved the submitted version.

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**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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