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Short paper

Sex differences in post cardiac arrest discharge locations

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Abstract

Background: We explored sex-based dierences in discharge location after resuscitation from cardiac arrest.

Methods: We performed a single-center retrospective cohort study including patients hospitalized after resuscitation from cardiac arrest from January 2010 to May 2020. We identified patients from a prospective registry, from which we extracted standard demographic and clinical variables. We explored favorable discharge location, defined as discharge to home or acute rehabilitation for survivors to hospital discharge. We tested the association of sex with the residuals of a multivariable logistic regression built using bidirectional selection to control for clinically relevant covariates.

Results: We included 2,278 patients. Mean age was 59 (SD 16), 40% were women, and 77% were admitted after out-of-hospital cardiac arrest. A total of 970 patients (43%) survived to discharge; of those, 607 (63% of survivors) had a favorable discharge location. Female sex showed a weak independent association with unfavorable discharge location (adjusted OR 0.94 (95%CI 0.89–0.99)).

Conclusions: Our results suggest a possible sex-based disparity in discharge location after cardiac arrest.

Keywords: Sex, Bias, Cardiac arrest

1. Introduction

Sex-based disparities have been observed in multiple aspects of cardiac arrest care. While women are more likely to survive to hospital admission after out-of-hospital cardiac arrest,[1] they are also more likely to die after withdrawal of life sustaining therapies (WLST) even when accounting for patient and arrest characteristics.[2,3] Women are also less likely to receive guideline-concordant interventions such as layperson cardiopulmonary resuscitation (CPR) and epinephrine.[4–6] The association of sex with post-acute cardiac arrest care has not been explored. Favorable discharge location is an independent predictor of long term survival.[7]

In this paper, we explore if unexplained sex differences exist in discharge location using a large single-center cohort. As secondary end-points, we explored sex-based differences in survival to hospital discharge and functionally favorable survival to discharge.

2. Methods

2.1. *Study Cohort*

We performed a retrospective observational cohort study including adults ⩾18 years of age hospitalized at a single academic medical center after resuscitation from in- and out-of-hospital cardiac arrest (IHCA and OHCA) between January 2010 and May 2020. We maintain a prospective registry of patients treated by our Post-Cardiac Arrest Service that includes demographic, clinical and arrest-specific characteristics and outcomes. We excluded patients who arrested due to primary neurological causes or trauma.[8] The

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University of Pittsburgh Human Research Protection Office approved this study.

2.2. Outcomes of Interest

Our primary outcome of interest was discharge location among survivors to hospital discharge. We treated this as a dichotomous outcome, and considered discharge to home or acute rehabilitation to be favorable locations (vs. discharge to a skilled nursing facility, long term acute care, or hospice) based on prior research associating this classification of discharge location with long-term post-arrest outcome.[7] As secondary outcomes, we explored sex differences in WLST for perceived poor neurological prognosis and overall survival to hospital discharge. In this work, we hypothesized that once accounting for medical covariates, there should be no unexplained difference in discharge disposition across arrest locations (IHCA and OHCA) and sex. Any remaining association of sex with the adjusted outcome is assumed to be due to confounders such as socioeconomic status.

2.3. Covariates

From our prospective registry, we abstracted sex and clinical covariates: age, witnessed arrest (0.04% missing), bystander cardiopulmonary resuscitation (CPR), arrest location and duration in minutes (4.74 % missing), number of doses of epinephrine administered (5.18% missing), arrest etiology,[8] initial ventricular tachycardia or fibrillation, cardiac catheterization, Charlson Comorbidity Index (CCI), and global illness severity, which we operationalized as Pittsburgh Cardiac Arrest Category (PCAC)[9] (9.79% missing). We also included modified Rankin Scale score (mRS - dichotomized as 0–2 vs 3–5) at discharge and hospital length of stay (LOS). Finally, we collected socioeconomic factors considered potential confounders: home environment (lives at home with friends or family vs. lives alone) and insurance status (private, public, or uninsured - 16.29% missing).

2.4. Statistical analysis

We imputed missing values by predictive regression based on other observed covariates. As a post hoc sensitivity analysis, we performed a complete case analysis. We used descriptive statistics to summarize cohort characteristics: χ^2 tests to compare categorical variables and Kruskal–Wallis tests to compare continuous variables.

To test for unexplained outcome differences across sex, we used adjusted logistic regression models with bidirectional selection. This iterative approach adds the feature which leads to best improvement of the model at each step (forward selection) and then removes any feature that no longer significantly improves prediction (backward selection). We used this approach because it excludes non-predictive covariates and helps minimize multicollinearity.

Finally, we tested the association between the residuals of the model built on the selected covariates, and sex using an ordinary least squares (OLS) regression. Studying this relationship after adjusted logistic regression quantifies any remaining sex difference.[10] If sex disparities were observed, we repeated this analysis with all covariates including socioeconomic covariates. This allows to test if available socioeconomic information explains the remaining sex difference. All analyses were performed using Python (v3.7) with statsmodel and scikit-learn libraries.

As a model sensitivity analysis, we present in Supplementary the result of a logistic regression built on the aggregation of the covariates selected by the bidirectional selection and sex.

3. Results

3.1. Cohort

Overall, 2,278 patients met criteria for inclusion, of whom 970 (43%) survived to hospital discharge and were included in our primary analysis. Of survivors to discharge, 607 (63%) had a favorable discharge location. Population characteristics are shown in Tables 1 and 2. Female sex was negatively associated with favorable discharge location (58% vs 65%, P = 0.04) in unadjusted analysis. After bidirectional selection on all discharge covariates, our adjusted model included age, catheterization, other non cardiac etiology, CCI, LOS, mRS, PCAC, and witnessed collapse. After adjustment, sex remained independently associated with location (P = 0.03) (Table 3) and women were less likely to have a favorable discharge location. Table 4 shows this difference is driven by a larger proportion of women admitted in skilled nursing facilities. In a secondary analysis, the difference remained when insurance status and home environment were added as inputs of the logistic regression model with bidirectional selection. Results were similar in our complete case and full logistic regression sensitivity analyses (see Supplementary).

3.2. Secondary outcomes

Prior to discharge, 668 patients (29%) had WLST, of whom 265 were women and 403 were men (P = 0.67). Sex was not independently associated with WLST. Of 1,610 patients who did not have WLST, 970 (60%) survived to discharge, of whom 378 were women and 592 were men (P = 0.08). Sex was not independently associated with survival to discharge.

4. Discussion

In this study, we found women are less likely to have a favorable discharge location after resuscitation from cardiac arrest. This difference remains when controlling for medically relevant covariates, as well as for socioeconomic variables that have been associated to discharge location following stroke.[11,12] Our findings identify a potential sex disparity in discharge location and call for future work to discover its causes and delineate potential changes to post-arrest care. Importantly, we have previously shown that discharge location is significantly associated with increased survival after controlling for potential confounders,[7] which emphasizes the clinical relevance of the observed difference. Discharge locations might also be a component in observed sex difference in long term quality of life.[13]

Our study relies on a single-center cohort. To contextualize our findings, we studied sex differences in outcomes that have been previously studied in the literature: WLST, and survival to hospital discharge. Past studies that analyze multiple centers have found women are more likely to experience WLST overall, and WLST prior to post-arrest day 3.[2,3] Sex differences have also been found in cardiac arrest survival, yet the previous conclusions are mixed. Some studies have found men are more likely to survive,[4] while other studies suggest that adjustment for presenting rhythm reduces or eliminates this difference.[14] In the cohort analyzed for this study, we find no sex differences in WLST or survival to hospital discharge. These findings suggest that sex disparities in post-arrest care in the center studied are lower than those observed in average, which underscores the relevance of the findings presented for sex

Table 1 – Baseline characteristics differentiated by sex. Median and interquartile differences are reported for continuous covariates, and absolute numbers with relative category frequencies are shown for categorical covariates. χ^2 tests were used to compare categorical variables and Kruskal–Wallis tests for continuous variables.

	Admission				Discharge			
Covariates	Cohort	Men	Women	P value	Cohort	Men	Women	P value
Number Patients	2,278	1,357	921	–	970	592	378	–
Age (Years)	61 (21.0)	61 (20.0)	60 (23.0)	0.748	61 (19.0)	61 (16.25)	60 (23.00)	0.339
CCI[*]	1.0 (3.0)	1 (3.0)	1 (2.0)	0.248	1.0 (2.0)	1.0 (2.0)	1.0 (2.0)	0.405
Arrest out-of-hospital (%)	1748 (76.73)	1028 (75.76)	720 (78.18)	0.197	702 (72.47)	424 (71.62)	279 (73.81)	0.503
Initial VT/VF[a] (%)	772 (33.89)	497 (36.62)	275 (29.86)	0.001	490 (50.52)	316 (53.38)	174 (46.03)	0.030
Etiology (%)				< 0.001				0.001
ACS[b]	353 (15.50)	239 (17.61)	114 (12.38)	–	219 (22.58)	159 (26.86)	60 (15.87)	–
Respiratory	341 (14.97)	169 (12.45)	172 (18.68)	–	121 (12.47)	67 (11.32)	54 (14.29)	–
Other cardiac[c]	371 (16.29)	229 (16.88)	142 (15.42)	–	218 (22.47)	125 (21.11)	93 (24.60)	–
Other non cardiac[d]	642 (28.18)	365 (26.90)	277 (30.08)	–	242 (24.95)	134 (22.64)	108 (28.57)	–
Unknown	571 (25.07)	355 (26.16)	216 (23.45)	–	170 (17.53)	107 (18.07)	63 (16.67)	–
Arrest duration (Minutes)	12 (21.0)	12 (21.0)	13 (21.0)	0.841	8 (12.5)	8 (12.0)	6.5 (13.0)	0.863
Bystander CPR[e] (%)	1108 (48.64)	664 (48.93)	444 (48.21)	0.752	413 (42.58)	259 (43.75)	154 (40.74)	0.148
Witnessed (%)	1025 (45.02)	624 (45.98)	401 (43.59)	0.526	419 (43.20)	270 (45.61)	149 (39.42)	0.159
Epinephrine (Number of doses)	2 (3.0)	2 (3.0)	2 (3.0)	0.248	1 (2.0)	1 (2.0)	1 (2.0)	0.578
PCAC[f] (%)				0.105				0.374
1	534 (25.99)	318 (25.75)	216 (26.34)	–	463 (52.14)	274 (50.46)	189 (54.78)	–
2	399 (19.42)	261 (21.13)	138 (16.83)	–	267 (30.07)	174 (32.04)	93 (26.96)	–
3	204 (9.93)	117 (9.47)	87 (10.61)	–	93 (10.47)	58 (10.68)	35 (10.14)	v
4	918 (44.67)	539 (43.64)	379 (46.22)	–	65 (7.32)	37 (6.81)	28 (8.12)	–
Catheterization (%)	596 (26.16)	390 (28.74)	206 (22.37)	0.001	412 (42.47)	275 (46.45)	137 (36.24)	0.002
Temperature Treatment (%)				0.695				0.565
36 °C	644 (28.27)	370 (27.27)	274 (29.75)	–	244 (25.15)	147 (24.83)	97 (25.66)	–
33 °C	767 (33.67)	472 (34.78)	295 (32.03)	–	204 (21.03)	135 (22.80)	69 (18.25)	–
Active Normothermia	31 (1.36)	18 (1.33)	13 (1.41)	–	13 (1.34)	7 (1.18)	6 (1.59)	–
No TTM[g]	694 (30.47)	409 (30.14)	285 (30.94)	–	458 (47.22)	270 (45.61)	188 (49.74)	–
Other[h]	142 (6.23)	88 (6.48)	54 (5.87)	–	51 (5.26)	33 (5.58)	18 (4.76)	–

[a] Ventricular Tachycardia or Fibrillation.
[b] Acute Coronary Syndrome.
[c] Intrinsic arrythmia, arrythmia secondary to cardiomyopathy, structural heart disease, left ventricule failure, right ventricule failure.
[d] Toxicological, airway obstruction, exsanguination, distributive shock, metabolic derangement.
[e] Cardio Pulmonary resuscitation.
[f] Pittsburgh Cardiac Arrest Category.
[h] Other targeted temperature.
[g] *Temperature Treatment Management.*
[*] Charlson Comorbidity Index.

Table 2 – Discharge characteristics differentiated by sex - Continued. Median and interquartile differences are reported for continuous covariates, and absolute numbers with relative category frequencies are shown for categorical covariates. χ^2 tests were used to compare categorical variables and Kruskal–Wallis tests for continuous variables.

	Discharge			
Covariates	Cohort	Men	Women	P value
Insurance status (%)				0.432
None	14 (1.72)	9 (1.85)	5 (1.54)	–
Private	714 (87.93)	433 (88.91)	281 (86.46)	–
Public	84 (10.34)	45 (9.24)	39 (12.00)	–
Hospital Length of Stay (days)	13 (15.0)	13 (16.25)	14 (13.0)	0.727
mRS[*] score (%)				0.269
0–2	280 (28.87)	179 (30.24)	101 (26.72)	–
3–5	690 (71.13)	413 (69.76)	277 (73.28)	–
Presence of a family member (%)	955 (98.45)	581 (98.14)	374 (98.94)	0.473

[*] modified Rankin Scale.

Table 3 – Multivariable logistic regression of baseline factors (after bidirectional selection) and their association with discharge location, and ordinary least square model of the association between its residuals and sex (last row).

	Discharge		
Factors	OR[*]	95 % CI	P value
Age	0.97	[0.95, 0.98]	< 0.001
Other cardiac etiology[a]	1.63	[1.12, 2.39]	0.011
Catheterization	1.75	[1.25, 2.46]	0.001
CCI[b]	0.88	[0.79, 0.97]	0.009
LOS[c]	0.98	[0.97, 0.99]	< 0.001
mRS[d]	0.18	[0.11, 0.29]	< 0.001
PCAC[e]	0.81	[0.69, 0.95]	0.008
Witnessed[f]	1.44	[1.04, 2.00]	0.028
Sex[g]	0.94	[0.89, 0.99]	0.030

[*] Odd Ratio
[a] Reference: Other etiologies.
[b] Charlson Comorbidity Index.
[c] Length Of Stay.
[d] modified Rankin Scale, Reference: 0–2.
[e] Pittsburgh Cardiac Arrest Category.
[f] Reference: Non witnessed.
[g] Reference: Men.

Table 4 – Post cardiac outcomes differentiated by sex. Absolute numbers and percentage are reported. χ^2 tests were used to compare outcomes in the populations at risk, ie WLST was compared in the whole cohort, survival for non WLST patients and discharge location in the survivor population.

Outcomes	Total	Men	Women	P value
WLST[*]	668 (29.32)	403 (29.70)	265 (28.77)	0.668
Death	640 (28.09)	362 (26.68)	278 (30.18)	0.083
Discharge Location				
Favorable	607 (26.65)	386 (28.44)	221 (24.00)	0.041
Home	398 (17.47)	248 (18.28)	150 (16.29)	0.538
Acute rehabilitation	209 (9.17)	138 (10.17)	71 (7.71)	0.111
Unfavorable	363 (15.94)	206 (15.18)	157 (17.05)	0.041
Skilled nursing facility	207 (9.09)	110 (8.11)	97 (10.53)	0.011
Long term acute care	69 (3.03)	39 (2.87)	30 (3.26)	0.504
Hospice	40 (1.76)	22 (1.62)	18 (1.95)	0.527
Other[a]	47 (2.06)	35 (2.58)	12 (1.30)	0.075

[a] Discharged to another acute in-patient facility, jail or psychiatric hospitalization.
[*] Withdrawal of Life Sustaining Therapies.

disparities in discharge disposition, and emphasizes the importance of studying disparities in this outcome across medical centers.

Our study has several limitations. First, it has to be emphasized that while the studied cohort includes all post-arrest admissions to a large hospital over a period of 10 years, providing a unique opportunity for analysis, this is a relatively small cohort from a statistical perspective. Such a cohort only allows observational analysis without correcting for multiple tests. Moreover, when deriving conclusions from this analysis, it is important to remember that hospitals' characteristics may impact survival.[15] Therefore, generalizability to external cohorts could be limited. One specific characteristic of this hospital is that patients are transferred to it from local hospitals, which might lead to an over-representation of severe conditions in the studied cohort. Moreover, it should also be noted that while we consider all medically relevant covariates in the available data, we cannot discard the possibility that unmeasured medical factors might influence the observed differences. Additionally, our analytical approach separated biological covariates from socioeconomic factors. This precluded exploration of potential interactions between these groups of predictors. Another limitation concerns the definition of positive outcome: because we could not reliably determine which patients were residing in a long term acute care or skilled nursing facility prior to arrest, patients returning to the same location might receive an unfavorable label. Finally, our insurance data does not contain details regarding the services covered by each plan, and we only study differences in private vs. public coverage. A finer granularity of this information could reveal that socioeconomic sex differences leading to insurance disparities explain some of the observed phenomena.

5. Conclusion

We identified statistically significant sex differences in discharge location following cardiac arrest. These differences were not explained by measured covariates, and because discharge location is independently associated with long-term outcomes after cardiac arrest,[7] such differences reflect a potentially addressable disparity. Understanding social and medical origins of these differences is a necessary step towards better training and provision of care, and further studying these disparities is necessary to eliminate the observed gap.

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Disclosures

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.resplu.2021.100185.

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