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ORIGINAL WORK

Mortality Following Diagnosis of Nontraumatic Intracerebral Hemorrhage Within an Integrated "Hub-and-Spoke" Neuroscience Care Model: Is Spoke Presentation Noninferior to Hub Presentation?

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Abstract

Background: Practice guidelines recommend that patients with intracerebral hemorrhage (ICH) be treated in units with acute neuroscience care experience. However, most hospitals in the United States lack this degree of specialization. We sought to examine outcome differences for patients with nontraumatic ICH presenting to centers with and without advanced neuroscience care specialization.

Methods: This was a retrospective study of adult patients presenting with nontraumatic ICH between 1/1/2011 and 9/30/2020 across 21 medical centers within Kaiser Permanente Northern California, an integrated care system that employs a "hub-and-spoke" model of neuroscience care in which two centers service as neuroscience "hubs" and the remaining 19 centers service as referral "spokes." Patients presenting to spokes can receive remote consultation (including image review) by neurosurgical or neurointensive care specialists located at hubs. The primary outcome was 90-day mortality. We used hierarchical logistic regression, adjusting for ICH score components, comorbidities, and demographics, to test a hypothesis that initial presentation to a spoke medical center was noninferior to hub presentation [defined as an odds ratio (OR) with an upper 95% confidence interval (CI) limit of 1.24 or less].

Results: A total of 6978 patients were included, with 6170 (88%) initially presenting to spoke medical centers. The unadjusted 90-day mortality for patients initially presenting to spoke versus hub medical centers was 32.2% and 32.7%, respectively. In adjusted analysis, presentation to a spoke medical center was neither noninferior nor inferior for 90-day mortality risk (OR 1.21, 95% CI 0.84–1.74). Sensitivity analysis excluding patients admitted to general wards or lacking continuous health plan insurance during the follow-up period trended closer to a noninferior result (OR 0.99, 95% CI 0.69–1.44).

Conclusions: Within an integrated "hub-and-spoke" neuroscience care model, the risk of 90-day mortality following initial presentation with nontraumatic ICH to a spoke medical center was not conclusively noninferior compared with

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initial presentation to a hub medical center. However, there was also no indication that care for selected patients with nontraumatic ICH within medical centers lacking advanced neuroscience specialization resulted in significantly inferior outcomes. This finding may support the safety and efficiency of a "hub-and-spoke" care model for patients with nontraumatic ICH, although additional investigations are warranted.

Keywords: Hemorrhagic stroke, Health care systems, Neurosciences

Introduction

Approximately 63,000 people develop nontraumatic intracerebral hemorrhage (ICH) annually in the United States, with a 30-day case mortality rate of 30–35% [1]. Practice guidelines recommend that patients with ICH be treated in units with acute neuroscience care experience, and on-site neurointensivist coverage within a 24-h dedicated neuroscience intensive care unit (ICU) is a core criterion for comprehensive stroke center certification by the American Heart Association and American Stroke Association [2, 3]. These recommendations are based on observational studies that indicate that treatment of patients with nontraumatic ICH in dedicated neuroscience ICUs and stroke units, compared with general ICUs or other wards, is associated with improved outcomes [4–6].

However, despite the expansion of dedicated neuroscience units in the wake of these recommendations [7], overall observed mortality from ICH has not changed appreciably over the past several decades [1, 8–10]. Furthermore, many of the interventions commonly used within neuroscience ICUs for patients with nontraumatic ICH lack clear evidence of benefit, including aggressive blood pressure control [11, 12], intracranial pressure monitoring [13, 14], and thrombolytic-assisted removal of intraventricular hemorrhage [15]. Although neurosurgical intervention appears beneficial for certain subtypes of ICH (infratentorial location with neurologic deterioration) and for certain complications (hydrocephalus), it is of unproven use for the vast majority of patients with nontraumatic supratentorial ICH [2, 16–20].

Accordingly, a large observational study examining outcomes of patients treated in specialty versus general ICUs between 2002 and 2005 failed to confirm a mortality benefit of neuroscience ICU over general ICU care for patients with ICH [21]. This finding may simply reflect the apparent ineffectiveness of specific advanced interventions, as noted above, but might also implicate improvements in general ICU care owing to education, treatment protocols, and neurocritical care exposure within neurology and critical care training programs in the United States, along with advances in telemedicine [22, 23]. As such, it may be reasonable to care for most patients with nontraumatic ICH outside of neuroscience ICUs, with selective referral.

To further explore whether selective referral to neurointensive care can achieve similar outcomes for patients with nontraumatic ICH, we aimed to examine mortality differences within an integrated health system employing a "hub-and-spoke" neuroscience care model, whereby most patients with nontraumatic ICH are cared for in "spoke" general ICUs following remote consultation by neurosurgical or neurointensive care specialists, with selective referral to "hub" neuroscience ICUs. Our hypothesis was that outcomes would be similar for emergency department (ED) patients diagnosed with acute nontraumatic ICH who initially presented to medical centers with 24/7 neuroscience ICU and neurointensivist availability (hub) compared with patients presenting to medical centers with neither neuroscience units nor on-site neurointensive care specialists (spokes).

Methods

Study Design and Setting

We performed a retrospective study of adult ED patients presenting with nontraumatic ICH between January 1, 2011, and September 30, 2020, across 21 medical centers within Kaiser Permanente Northern California (KPNC). KPNC is a private, nonprofit, integrated health care system that covers 4.4 million members, or approximately a third of the region's population. KPNC members have been found to be comparable to the surrounding population with respect to age, sex, race, and ethnicity [24]. KPNC has two (hub) neuroscience medical centers, both certified as comprehensive stroke centers by the American Heart Association (including 24/7 neuroscience ICU and neurointensivist availability), with an average combined annual ED visit volume of approximately 150,000. The remaining 19 medical centers serve as spokes, all of which have primary stroke center designation, provide care for patients with critical neurologic disease in "general" mixed medical-surgical ICUs, and have an average combined annual ED visit volume of 1 million. Two of the spokes are also designated trauma centers and provide on-call neurosurgical consultation. Patients with ICH are referred from spoke medical centers to hubs (or similarly enabled non-KPNC medical centers, when transfer to a KPNC hub would risk a delay in care) at the discretion of hub-based consulting neurointensivists and/or neurosurgeons. All care facilities (emergency, outpatient, inpatient) within KPNC use the same comprehensive integrated electronic health record (Epic, Verona, WI).

This article does not contain any studies with human participants or animals performed by any of the authors. For this type of study, formal consent is not required. The study was approved by the KPNC Institutional Review Board with a waiver of informed consent.

Study Population

Patient encounters were considered for study inclusion if they met all the following criteria: (1) 18 years or older; (2) presented to a KPNC ED between 1/1/2011 and 9/30/2020; (3) admitted to an inpatient bed at the presenting medical center or transferred to another medical center; (4) had an International Classification of Disease, 9th revision (ICD-9) and 10th revision (ICD-10) diagnosis code (ICD-9 for January 1, 2011 through September 30, 2015; ICD-10 for October 1, 2015, and later) for nontraumatic ICH (ICD-10 I61.x or 162.9, ICD-9 431.x or 432.9) and without a concomitant ICD-9 or ICD-10 code for trauma (ICD-9 800-4.x, 851-4.x; ICD-10 S06.x); and (5) underwent computed tomography (CT) of the brain in the ED. Patient encounters were excluded from the study if there was concomitant pregnancy, absence of intraparenchymal cerebral hemorrhage on CT imaging, or a suspected secondary cause of intraparenchymal hemorrhage based on concomitant CT evidence of primary subarachnoid hemorrhage, arterial-venous malformation, extra-axial hematoma, or bony fracture (see below). Additionally, in cases of multiple study eligible encounters by the same patient during the study period, to prevent overlapping 90-day outcome periods and repeated measurements, we did not include those encounters occurring within 90 days after an earlier included encounter.

Structured Electronic Data Variables

Using structured data present in the electronic health record, we recorded the following patient-level variables: age, sex, race, Elixhauser comorbidity index score (including the 29 component diagnostic groupings) [25], Kaiser Permanente health plan membership status, Glasgow Coma Scale (GCS) score (average of two lowest recorded values in the ED), active prescriptions for an anticoagulant medication (vitamin K antagonists, direct-acting oral anticoagulants, or low-molecular-weight heparins), anticoagulant reversal therapy administration in the ED, a do not resuscitate (DNR) order placed within 72 h of ED arrival, and disposition from the ED (admission to general ward, operating room, or ICU or transfer to another hospital). Although most patient transfers were to the neuroscience hub medical centers within the KPNC network, 7% of all patients presenting to spoke medical centers were transferred to non-KPNC medical centers, likely owing to indications for acute neurosurgical care and/or logistical limitations, and thus a complete accounting of neurosurgical interventions (or DNR orders within 72 h) was not available.

Natural Language Processing of Radiology Reports

Free text from the final radiology report was analyzed for the following intents: (1) to identify exclusion criteria (absence of intraparenchymal cerebral hemorrhage or suspected secondary causes of intraparenchymal hemorrhage) and (2) to abstract ICH score variables (hematoma volume $\geq$ 30 ml, presence of infratentorial hemorrhage, presence of intraventricular hemorrhage) [26]. Using an iterative process based on manual review of radiology report text, specific key words were identified for each intent along with several negative or positive modifiers (also tailored to each key word). A hierarchy of rules was then created based on these keywords and their modifiers to refine study eligibility criteria and determine the presence or absence of each ICH score variable (Supplemental Methods). The results of the text processing algorithms were subsequently validated against referential gold standard interpretation of 200 randomly sampled images by a board-certified neuroradiologist study investigator who was anonymized to the text processing methodology, results, and the original image interpretations. Hematoma volume was determined by using the ABC/2 method [27]. Interrater agreement was deemed acceptable if the percent agreement was 85% or greater.

Outcomes

The primary outcome was 90-day mortality using a composite mortality database, which integrates KPNC mortality records, California Department of Public Health Vital Records, and the National Death Index.

Analysis

We used hierarchical multivariable regression analysis to examine the association between initial presentation to a hub-or-spoke medical center ED (primary independent variable of interest) and 90-day mortality (dependent variable), adjusting for patient-level variables (age, sex, GCS score, additional ICH score components [hematoma volume $\geq$ 30 ml, presence of infratentorial hemorrhage, presence of intraventricular hemorrhage], Elixhauser comorbidity index score, active anticoagulation prescription, and receipt of an anticoagulant reversal agent in the ED), facility-level characteristics (24 h intensivist coverage, annual ICH volume quartile, inpatient neurosurgical services at "spoke" medical centers), and secular trends (calendar year), with random effects at the facility level. We assessed covariate interactions and added a statistically significant interaction term (active anticoagulation prescription and receipt of an anticoagulant reversal agent in the ED) to the final model. Regression analysis results were reported as odds ratios (ORs). Missing data were imputed by using Rubin's multiple imputation method [28]. Comparisons involving categorical variables were performed y using the χ^2 or Fisher's exact test, and comparisons of continuous variables by using the Wilcoxon rank-sum test. We also reported results with the Farrington and Manning risk-difference approach by using the same multivariable regression approach but structuring GCS score as a categorical variable (3–4, 5–12, and 13–15, as per the ICH score) with an indicator for GCS score missingness (risk-difference estimates are not available when using multiple imputation) [29]. Sensitivity analyses were performed for both approaches by excluding patients admitted to general ward beds (being unlikely to represent patients who would benefit from neurointensive care), patients without continuous active health plan membership during the 90-day outcome period (potential under adjustment for comorbidities and/or incomplete outcome capture), or both.

The primary analysis was a noninferiority assessment of 90-day mortality. We assumed a base mortality of 30.0% at neuroscience hub centers and a sample size of 7148 patients with a hub-to-spoke study patient ratio of 1:8, based on existing literature and preliminary data. Using an α of 0.025 and a one-sided score test (Farrington and Manning), we estimated 80% power to exclude a noninferiority margin of 4.7% at the upper 97.5% confidence interval (CI) corresponding to an OR of 1.24. This OR is below the range of benefit behind guideline support of neuroscience ICU care (OR 3.4, 95% CI 1.65–7.60) but is in line with literature suggesting equivalent outcomes between general ICU and neuroscience ICU care for patients with ICH (OR 1.0, 95% CI 0.79–1.28) [4, 21]. The analyses were performed by using Stata 17.0 (StataCorp, College Station, TX).

Results

There were 11,385,637 ED encounters during the study period. A total of 6978 patients with nontraumatic ICH were included in the study population, 6170 (88%) of whom presented to spoke medical center EDs (Fig. 1). The median age was 70 years and 47% of patients were women (Table 1). The median GCS score was 14 (interquartile range 10–15), 19% had an ICH volume ≥ 30 ml, 34% had intraventricular hemorrhage, and 14% were treated with an anticoagulant reversal therapeutic while in the ED. Patients presenting to spoke medical centers were older and more likely to have recent prescriptions for anticoagulants, have health plan insurance, and be transferred to another hospital from the ED. Although patients presenting to spoke medical centers were slightly more likely to have DNR orders placed within 72 h (28% versus 24%), this comparison does not account for the 7% of patients transferred from spoke EDs to non-KPNC

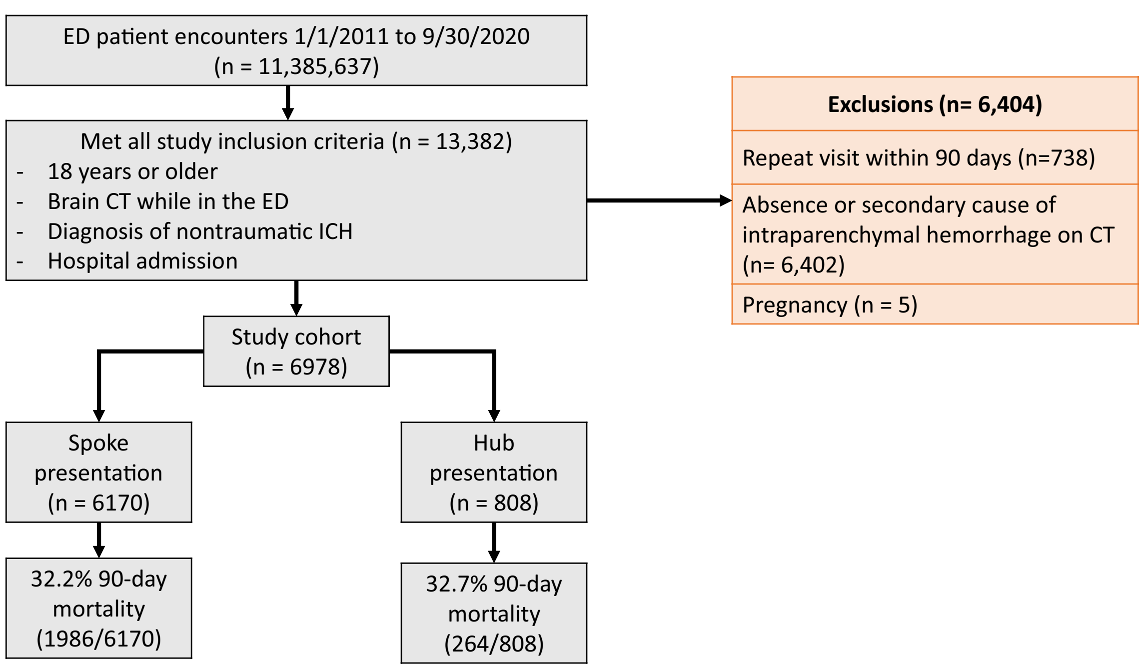

Fig. 1 Study cohort selection. *CT* computed tomography, *ED* emergency department, *ICH* intracerebral hemorrhage

Table 1 Patient characteristics

All		All		Spoke		Hub		*p* value
		n	%	*n*	%	*n*	%	
		6978	100	6170	100	808	100	
Characteristics								
Age	Median (IQR)	70	(58–81)	71	(59–81)	66	(54–78)	< 0.001
Sex	Female	3277	47	2893	47	384	48	0.73
Race/ethnicity	White	3232	46	2829	46	403	50	0.02
	Black	834	12	735	12	99	12	
	Hispanic	1030	15	905	15	125	15	
	Asian	1754	25	1590	26	164	20	
	Other	128	2	111	2	17	2	
ED disposition	General ward	1385	20	1223	20	162	20	< .0001
	ICU	3607	52	2997	49	610	76	
	OR	51	0.7	19	0.3	32	4	
	Transferred	1935	28	1931	31	4	0.5	
	To KPNC medical center	1522	22	1520	25	2	0.3	
	To non-KPNC medical center	413	6	411	7	2	0.3	
Health plan member	Yes	5328	76	4815	78	513	63	< .0001
GCS score in ED	Median (IQR)	14	(10–15)	14	(11–15)	14	(9–15)	0.0002
	3–4–4	460	7	388	6	72	9	0.03
	5–1–12	253	4	222	4	31	4	
	13–1–15	4702	67	4164	67	538	67	
	Missing	1563	22	1396	23	167	21	
ICH volume ≥ 30 ml	Yes	1301	19	1132	18	169	21	0.08
Intraventricular hemorrhage	Yes	2400	34	2102	34	298	37	0.11
Anticoagulant prescription*	Yes	1076	15	972	16	104	13	0.03
Anticoagulation reversal agent used	Yes	996	14	889	14	107	13	0.37
Elixhauser score	Median (IQR)	0	(0–7)	0	(0–7)	0	(0–6)	0.07
DNR order within first 72 hours**	Yes	1822	28	1626	28	196	24	0.02
90-day mortality	Yes	2250	32	1986	32	264	33	0.78

DNR do not resuscitate, *ED* emergency department, *GCS* Glasgow Coma Scale, *ICH* intracerebral hemorrhage, *ICU* intensive care unit, *KPNC* Kaiser Permanente Northern California, *OR* operating room

*Vitamin K antagonists, direct-acting oral anticoagulants, or low-molecular-weight heparins

**Excludes patients transferred to non-KPNC medical centers

medical centers. Compared with patients admitted to spoke ICUs, patients transferred from spoke EDs were younger, had a lower median GCS, were more likely to have ICH volume ≥ 30 ml or intraventricular hemorrhage, and were less likely to have health plan insurance or DNR orders placed within 72 h (12% versus 24%, not accounting for patients transferred to non-KPNC medical centers, Supplemental Data).

Interrater agreement between natural language processing of written radiology reports and blinded CT image review by a neuroradiologist was acceptable, yielding percent agreements of 87% for radiographic inclusion/exclusion criteria, 92% for the presence of intraventricular hemorrhage, 87% for ICH volume of 30 ml or greater, and 89% for infratentorial hemorrhage (Table 2).

The unadjusted 90-day mortality for patients initially presenting to spoke and hub medical centers was 32.2% (1,986/6,170) and 32.7% (264/808), respectively. The corresponding adjusted OR for 90-day mortality among patients presenting to spoke medical centers was 1.21 (95% CI 0.84–1.74, $p = 0.3$; Table 3), which failed to meet the prespecified noninferiority criteria of an upper 95% CI of 1.24 or less. Associations between 90-day mortality and other facility-level characteristics (24 h in-house intensivist coverage, quartile of annual ICH volume, inpatient neurosurgical services at spoke centers) were likewise statistically nonsignificant. Sensitivity

Table 2 Interrater agreement for imaging findings on computed tomography

Parameter	Percent agreement (%)	Kappa
Intraventricular hemorrhage	92	0.80
ICH volume of 30 ml or greater	87	0.66
Infratentorial hemorrhage	89	0.58
ICH score (range 0 to 3)	75	0.68 (weighted)
Study exclusions	87	0.65

Interrater agreement between natural language processing algorithm classification and blinded image review by a board-certified neuroradiologist

ICH intracerebral hemorrhage

analyses excluding patients admitted to general ward beds (unlikely to benefit from neurointensive care), patients without active health plan membership (potential incomplete risk adjustment and/or outcome capture) or both likewise failed to meet noninferiority criteria (Table 4), although point estimates trended closer to noninferiority (combined exclusion analysis OR 0.99, 95% CI 0.69–1.44). Alternative analyses using the risk-difference approach likewise failed to meet noninferiority criteria (i.e., an upper 95% CI of 4.7% or less: Table 5). An exploratory subgroup analysis of patients with high-risk characteristics (GCS score less than 13, ICH volume ≥ 30 ml, or intraventricular hemorrhage) did not reveal a clear 90-day mortality benefit to initial hub presentation (OR 1.33, 95% CI 0.81–2.17).

Discussion

In this study, we analyzed the comparative risk of 90-day mortality between patients with nontraumatic ICH who initially presented to the EDs of spoke medical centers (without on-site advanced neuroscience expertise) versus hub medical centers (with neurointensivists and a dedicated neuroscience ICU) within an integrated care delivery system. To our knowledge, this is the first study to analyze outcomes for this condition within an integrated hub-and-spoke care model. Although the results did not meet the hypothesized noninferiority criteria for presentation to a spoke medical center, potentially because the sample size was underpowered by a priori estimates, our findings do provide some support to the safety and efficiency of this care model given that the risk estimates largely centered around a null point estimate. It thus remains probabilistically likely that presentation to a spoke medical center ED was unlikely to result in significantly inferior outcomes among most patients with nontraumatic ICH, although a slightly greater risk among patients with high-risk characteristics cannot be excluded. It is also important to emphasize that the

Table 3 Multivariate (base) model for 90-day mortality

Parameter	OR	95% CI		*p* value
Presentation to a spoke medical center	1.21	0.84	1.74	0.30
Glasgow Coma Scale Score (per point)	0.80	0.78	0.81	< 0.001
ICH volume of 30 ml or greater	2.68	2.29	3.15	< 0.001
Intraventricular hemorrhage	2.03	1.77	2.33	< 0.001
Age				
spline1	1.01	0.99	1.03	0.28
spline2	1.05	0.98	1.11	0.14
spline3	0.80	0.52	1.23	0.31
spline4	1.50	0.65	3.46	0.34
Sex				
Male	Reference			
Female	0.83	0.73	0.94	0.004
Race/ethnicity				
White	Reference			
Black	0.61	0.49	0.76	< 0.001
Hispanic	0.83	0.68	1.00	0.053
Asian	0.57	0.48	0.67	0.000
Other	0.67	0.40	1.09	0.11
ED disposition				
Non-intensive care bed	Reference			
Intensive care bed	0.58	0.49	0.69	< 0.001
Operating room	0.37	0.18	0.76	0.007
Transfer to an acute care hospital	0.44	0.36	0.54	< 0.001
Active health plan membership	0.88	0.74	1.04	0.12
Recent anticoagulation prescription	1.70	1.25	2.31	0.001
Anticoagulation reversal agent treatment	1.87	1.32	2.66	< 0.001
Interaction term (recent anticoagulant prescription and anticoagulation reversal agent treatment)	0.33	0.20	0.53	< 0.001
Elixhauser comorbidity score	1.04	1.04	1.05	< 0.001
24 h in-house intensivist availability (spoke)	0.83	0.62	1.10	0.19
Annual ICH volume quartile				
Quartile 1 (lowest)	Reference			
Quartile 2	1.11	0.89	1.40	0.35
Quartile 3	1.11	0.87	1.41	0.40
Quartile 4 (highest)	1.17	0.92	1.50	0.21
Inpatient neurosurgical services (spoke)	1.12	0.78	1.61	0.54
Calendar year				
2011	Reference			
2012	1.10	0.79	1.51	0.58
2013	0.98	0.71	1.36	0.92
2014	0.90	0.66	1.24	0.53
2015	0.81	0.60	1.10	0.17
2016	0.86	0.64	1.16	0.33
2017	0.97	0.72	1.30	0.82
2018	0.84	0.63	1.13	0.24
2019	1.01	0.76	1.36	0.92
2020	0.85	0.62	1.16	0.30

Table 3 (continued)

Hierarchical multivariable logistic regression with random effects at the facility level. Missing data were imputed using Rubin's multiple imputation method

CI confidence interval, *ED* emergency department, *ICH* intracerebral hemorrhage, *OR* odds ratio

generalizability of our findings is limited by the study setting: a highly integrated care delivery system in which all spokes were designated primary stroke centers and had capacity for evaluation via remote consultation (including image review) by neurosurgical or neurointensive care specialists to determine which patients might benefit from care in a dedicated neuroscience unit.

To this last point, given that nearly one third of study patients presenting to spoke EDs were transferred to other medical centers, our findings should not be considered a direct comparison of outcomes among patients with ICH cared for in general versus neuroscience ICUs. Due to unmeasured variables driving selection of patients for transfer (e.g., patient-specific variables such as goals of care or provider-specific variance in thresholds for transfer), our data are not well suited to directly address this question. However, a reasonable corollary of our findings is that care of selected patients with nontraumatic ICH within general ICUs is likely safe, or at least not inferior to the degree suggested by prior evidence.

The landmark study that raised concern over inferior outcomes [4] reported higher adjusted hospital mortality (OR 3.4, 95% CI 1.7–7.6) for patients with ICH cared for in general versus neuroscience ICUs, adjusting for age, neurologic status, and institutional characteristics (volume of patients with ICH cared for annually, ICU size, full-time intensivist) [4]. A second study found that patients with ICH who were cared for in stroke units had 40% lower odds of death or disability at 3 months, compared with other types of wards [5]. A third single-center study suggested that creation of a neuroscience ICU improved outcomes among patients with ICH, although this conclusion was confounded by multiple simultaneous institutional changes [30]. Finally, treatment of patients with ICH at centers with increasing degrees of comprehensive stroke care

Table 4 Sensitivity analyses: adjusted odds of 90-day mortality for patients with nontraumatic intracerebral hemorrhage presenting to spoke versus neuroscience hub medical centers

Parameter	OR (95% CI)	*p* value*
90-day mortality (unadjusted)	0.98 (0.84–1–1.14)	0.77
90-day mortality (adjusted)		
Full cohort (Base model, Table 3)	1.21 (0.84–1–1.74)	0.30
Excluding patients admitted to general ward beds (sensitivity analysis #1)	1.14 (0.78–1–1.68)	0.50
Excluding patients without active health plan membership (sensitivity analysis #2)	1.08 (0.75–1–1.55)	0.68
Combined above exclusion criteria (sensitivity analysis #3)	0.99 (0.69–1–1.44)	0.97

Analysis performed using hierarchical multivariable logistic regression with random effects at the facility level, as per Table 3. Missing data were imputed using Rubin's multiple imputation method

CI confidence interval, *OR* odds ratio

* One-sided *p* value for a prespecified-specified noninferior marginal difference of + 4.7%

Table 5 Alternative analyses: adjusted risk differences in 90-day mortality for patients with nontraumatic intracerebral hemorrhage presenting to spoke versus neuroscience hub medical centers

Parameter	*n*	Hub medical center (%)	Spoke medical center (%)	Risk difference (95% CI)
90-day mortality (unadjusted)	6978	32.7	32.2	−0.5% (− 3.9 to 3.1%)
90-day mortality (adjusted)				
Full cohort (base model)	6978	29.7	32.6	+ 2.9% (− 2.2 to + 8.1%)
Excluding patients admitted to general ward beds (sensitivity analysis #1)	5593	26.8	28.9	+ 2.1% (− 3.2 to + 7.5%)
Excluding patients without active health plan membership (sensitivity analysis #2)	5971	36.5	37.9	+ 1.4% (- − 3.8% to + 6.7%)
Combined above exclusion criteria (sensitivity analysis #3)	4662	33.9	34.6	+ 0.7% (− 4.5 to + 5.9%)

Analysis performed using hierarchical multivariable logistic regression with random effects at the facility level as per Table 3, with modified treatment of the Glasgow Coma Scale Score as a categorical variable and a categorical indicator for missingness

CI confidence interval

capacity (comparable to the hubs in our study) has been associated with lower in-hospital mortality. However, no mortality differences were found when comparing care of patients with ICH at designated primary stroke centers (comparable to the spokes in our study) versus nondesignated centers, arguing against a dampening of the baseline risk owing to this factor in our study setting [31, 32].

However, in a large examination of patient outcomes following care for common conditions within specialty or general ICUs [21], no clear mortality benefit was associated with neuroscience ICU care for patients with ICH as compared to care within general ICUs (adjusted OR 1.0, 95% CI 0.79–1.28) [21]. This range of odds is much closer to our findings, specifically for the sensitivity analyses that excluded patients admitted to non-ICU settings (adjusted OR 0.99, 95% CI 0.69–1.44), and stands in somewhat stark contrast to the seminal article by Diringer et al. [4] noted above. The older data examined in the study by Diringer et al. [4] (late 1990s) may explain some of this discrepancy, perhaps owing to increased application of neurocritical care principles within general ICU practice settings over time and, most pertinent to our study, better selection of patients with ICH for care within general ICUs [22, 23]. In support of this contention, a more recent single-center study found that treatment in a neurocritical care unit and/or by a neurointensivist did not impact outcomes among critically ill patients with ICH [33]. It is thus likely that both our findings and the report by Lott et al. [21] better represent the current state of ICH care within general ICUs in the United States.

One limitation of our study was that we were unable to reliably identify downstream neurosurgical interventions because 7% of patients presenting to spoke medical centers were transferred from the ED to medical centers outside of our integrated health care system for acute neuroscience care, likely owing to a high likelihood of needing emergent neurosurgical intervention. Thus, we cannot ascertain the degree to which neurosurgical interventions may have contributed to outcomes and differed between patients presenting to spoke and hub medical centers. Although neurosurgical intervention is of uncertain benefit for most patients with nontraumatic supratentorial ICH, a meta-analysis of individual patient data from randomized controlled trials suggests that certain subgroups of patients with supratentorial ICH, such as those with a GCS of 9–12 or hematoma volumes between 20 and 50 ml, may benefit from neurosurgery [2, 16–20]. In addition, emerging evidence indicates a larger potential role for surgical therapy via minimally invasive, stereotactic, and/or endoscopic clot evacuation [34, 35]. To these points, however, we did conduct an exploratory subgroup analysis of patients with high-risk characteristics, which did not reveal a clear mortality benefit to initial hub presentation.

Another limitation is that we were unable to fully account for differences in thresholds to provide life sustaining treatments and/or pursue withdrawal of care as pertains to the 90-day mortality outcome [36]. This is a complex and time-varying variable influenced by patient and family values as well as clinicians' perspectives on prognosis, all of which also likely impacted decisions surrounding transfer for neuroscience care, as noted above. Although we did find that a slightly higher percentage of patients presenting to spoke medical centers had "early" DNR orders placed within 72 h (28% vs 24%), these estimates excluded patients transferred to non-KPNC medical centers, and imputation of these missing data (using the 12% early DNR order incidence observed among patients transferred to KPNC medical centers) rendered the difference nonsignificant (27% vs 24%, $p=0.09$). Additionally, recent evidence has found that hospital-level utilization of early DNR orders among patients with ICH may not be a reliable proxy for less aggressive care and higher in-hospital mortality risk, or at least not to the degree suggested by older data [37, 38]. Regardless, any such differences did not manifest in an appreciable inferiority of spoke presentation in terms of 90-day mortality, and thus do not alter conclusions concerning the apparent safety of this integrated hub-and-spoke acute neuroscience care delivery model.

Additional limitations inherent to the retrospective study design include the potential for incomplete capture of study eligible patients through reliance on the diagnostic codes, incomplete specificity in case identification with the use of the same diagnostic codes, inability to extended outcome analyses beyond crude mortality (e.g., functional outcomes), and risk adjustment based on electronically extracted variables, including text analysis of radiology reports. Regarding the use of diagnostic codes for case identification, it is unlikely that there was a differential coding bias between emergency physicians practicing at hub-or-spoke medical centers such that representative patients were unequally distributed. Additionally, we were able to improve on the specificity of case identification through radiology text analysis, thereby increasing confidence in the validity of our results, albeit at the cost of anticipated study power. Although determination of radiographic ICH score elements was based on free text processing of the written radiology report, given the impracticality of manual chart review, agreement with gold standard blinded neuroradiologist interpretation was good to excellent. Study strengths include a relatively large sample size compared with other related studies on this topic, inclusion of non-ICU bound patients to account for any potential bias in treatment or intensity of monitoring between spokes and hubs, and risk adjustment using ICH score components.

Conclusions

Within an integrated hub-and-spoke neuroscience care model, characterized by remote neurosurgical consultation capacity and universal stroke center certification, we were unable to demonstrate that the risk of 90-day mortality following diagnosis of nontraumatic ICH at a spoke medical center ED was noninferior to the presentation and diagnosis at a hub medical center ED. However, we likewise found no indication that care for selected patients with ICH within medical centers lacking neuroscience specialization resulted in significantly inferior outcomes. This finding may support the safety and efficiency of this hub-and-spoke care model for patients with nontraumatic ICH, although additional investigations are warranted.

Supplementary Information

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Author contributions

The final manuscript was approved by all authors: study concept and design (DGM, JH, MER, ASR), acquisition of the data (JH, DCS), analysis and interpretation of the data (DGM, JH, MER), drafting of the article (DGM), critical revision of the article for important intellectual content (JH, DCS, ASR, MER), and statistical expertise (JH, MER, DGM).

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Conflict of interest

The authors declare that they have no conflicts of interest.

Ethical Approval/Informed Consent

We confirm adherence to ethical guidelines and indicate ethical approvals (institutional review board) and use of informed consent and have included a statement regarding institutional review board approval.

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