


ORIGINAL WORK



Worldwide Organization of Neurocritical Care: Results from the PRINCE Study Part 1

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Abstract

Introduction: Neurocritical care focuses on the care of critically ill patients with an acute neurologic disorder and has grown significantly in the past few years. However, there is a lack of data that describe the scope of practice of neuro-intensivists and epidemiological data on the types of patients and treatments used in neurocritical care units worldwide. To address these issues, we designed a multicenter, international, point-prevalence, cross-sectional, prospective, observational, non-interventional study in the setting of neurocritical care (PRINCE Study).

Methods: In this manuscript, we analyzed data from the initial phase of the study that included registration, hospital, and intensive care unit (ICU) organizations. We present here descriptive statistics to summarize data from the registration case report form. We performed the Kruskal–Wallis test followed by the Dunn procedure to test for differences in practices among world regions.

Results: We analyzed information submitted by 257 participating sites from 47 countries. The majority of those sites, 119 (46.3%), were in North America, 44 (17.2%) in Europe, 34 (13.3%) in Asia, 9 (3.5%) in the Middle East, 34 (13.3%) in Latin America, and 14 (5.5%) in Oceania. Most ICUs are from academic institutions (73.4%) located in large urban centers (44% > 1 million inhabitants). We found significant differences in hospital and ICU organization, resource allocation, and use of patient management protocols. The highest nursing/patient ratio was in Oceania (100% 1:1). Dedicated Advanced Practiced Providers are mostly present in North America (73.7%) and are uncommon in Oceania (7.7%) and the Middle East (0%). The presence of dedicated respiratory therapist is common in North America (85%), Middle East (85%), and Latin America (84%) but less common in Europe (26%) and Oceania (7.7%). The presence of dedicated pharmacist is highest in North America (89%) and Oceania (85%) and least common in Latin America (38%). The majority of respondents reported having a dedicated neuro-ICU (67% overall; highest in North America: 82%; and lowest in Oceania: 14%).

Conclusion: The PRINCE Study results suggest that there is significant variability in the delivery of neurocritical care. The study also shows it is feasible to undertake international collaborations to gather global data about the practice of neurocritical care.

Keywords: Neurocritical care, Observational study, Outcomes, Critical care, Prospective

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See complete listing of the PRINCE Study Investigators in Appendix A (Supplementary material).

Introduction

Neurocritical care is a subspecialty of critical care medicine that focuses on the care of critically ill patients with primary or secondary neurosurgical or neurological problems [1]. It is also dedicated to the advancement of such care [2]. The development of neurocritical care evolved from

the recognition that primary brain injuries are affected by systemic alterations, e.g., hypoxia or fever and ongoing events in the brain (the so-called secondary injuries), when not recognized and treated promptly. The field has evolved from a primary focus on the post-operative care of neurosurgical patients to the broader resuscitation of patients with severe brain insults, patients with medical conditions that affect the brain, e.g., cardiac arrest and disorders of the spinal cord or peripheral nerves, e.g., ascending polyneuropathy. The individuals that are specially trained to deal with these complex issues are called neurointensivists.

Neurocritical care has grown enormously in the past few years [3, 4]. Such growth was enhanced by the creation of the Neurocritical Care Society (NCS) in 2003 with the support of the Society of Critical Care Medicine [5]. The NCS is a multidisciplinary nonprofit organization that currently has over 1000 members from more than 24 countries around the world. In addition, in 2005 the medical subspecialty of neurocritical care achieved a major milestone in the USA when it gained full acceptance by the United Council of Neurological Subspecialties, which is a nonprofit organization committed to the establishment of training standards for neurological subspecialty fellowship programs [6, 7]. Despite these advances, there is limited data on the scope of practice of neurointensivists and epidemiological data on the types of patients and treatments used in neurocritical care units (NCCU) worldwide. For example, there is the perception that neurocritically ill patients in the USA are usually cared for in dedicated NCCUs compared to other regions of the world where those patients are cared for in mixed-type units. To address these issues, we designed a multicenter, international, point-*PRE*valence, cross-sectional, prospective, observational, non-interventional study *In NeuroCritical care* (PRINCE Study). We wanted to determine whether there is geographic variability in the scope of practice of neurointensivists and the delivery of neurocritical care. In this manuscript, we describe data from the first part of the PRINCE Study, which included registration and a description of hospital and overall neurocritical care services organization. We believe that presenting this information is important as this provides the first glimpse into the organization of neurocritical care in various regions of the world and will serve as the starting point for further studies and discussions regarding neurocritical care practice and resource allocation. We have followed the recommendations of the STROBE Statement checklist [8].

Study Design

Participating Sites

Most participating sites are members of the Neurocritical Care Research Network (NCRN) [9]. NCS created the NCRN in 2010 to enhance international and multicenter

research collaborations in neurocritical care. All NCRN-member sites received an e-mail invitation. In addition, we sent electronic invitations to members of the Neurointensive care section of the European Society of Intensive Care Medicine (ESICM), the Latin American Brain Injury Consortium (LABIC), the Clinical Trials Group of the Australian and New Zealand Intensive Care Society (ANZICS-CTG), the Canadian Critical Care Trials Group (CCCTG), Initiative of German Neurointensive Trial Engagement (IGNITE) of the German Neurointensive Care Society, the Chinese University of Hong Kong, and the Neurocritical Care Middle East and North Africa (NCC-MENA) chapter of the International Pan Arab Critical Care Medicine Society. Participation was voluntary and uncompensated.

Participating sites registered 4 months before scheduled data collection and obtained IRB/Ethics approval. Site investigators entered information about activities performed in their Intensive Care Units (ICUs) on all admissions on the opening study day (7/21/2014). Investigators collected data on specific care activities they performed on the subjects during their first 7 days of admission or discharge (whichever came first) from their ICUs. All the variables that were collected are validated in the neurological literature and accepted by the National Institute of Neurological Disorders and Stroke as part of the Common Data Elements project [10]. The IRB/Ethics Committee at the Baylor College of Medicine (BCM) in Houston, TX, approved a waiver of consent for the PRINCE Study. All participating sites obtained IRB/Ethics approval at their respective institutions before data collection and after the central approval at BCM.

Data Collection

PRINCE Study data were collected and managed using REDCap (Research Electronic Data Capture) tools hosted at the BCM [11, 12]. The PRINCE database had a built-in audit trail that automatically logged all user activities and logged all pages viewed by every user, including contextual information (e.g., the project or record being accessed). In addition, the database implemented authentication to validate the identity of end users that logged into the system.

We created six Case Report Forms (CRFs) for investigators to fill out (Appendix B in Supplementary material). CRF1 was completed upon registration. CRFs 2–5 were completed between days 1 and 7 of the acute date collection period. CRF 6 was completed at the time of hospital discharge. CRF1 includes data on hospital and ICU organization. We are presenting here our analysis of data from CRF1 and will be describing data from CRFs 2–6 in a separate publication [13].

Training and Monitoring

We created training videos and PowerPoint presentations that were submitted electronically to all participating investigators. In addition, we held weekly teleconferences with participating sites for 1 month before the data collection start date. During these teleconferences, we reviewed the study protocol and addressed specific instructions for data collection and entry and all concerns raised by the participating sites. We did not monitor data collection and entry. However, we evaluated incongruous data and outlier values and reconciled those with site investigators. Outliers were defined as values that fell outside two standard deviations from the mean. Incongruous data related to those who were entered using the wrong allowed units or measures.

Once the data entry period was completed, we initiated the data reconciliation process. The latter took 8 months of many e-mail and WhatsApp® correspondence to ensure that all queries were addressed. In addition, because several sites required data use agreements prior to data entry for Part 2 of PRINCE, we needed to comply with their legal requirements. Specifically, most of those documents indicated that sites needed to be contacted at the end of the data-collection period and prior to publication to ensure that no identifiable information was entered. This process took another 12 months. Moreover, The PRINCE PI (JIS) relocated in 2017 and had to renegotiate access to the study database which was housed at the BCM. The latter took 18 more months.

Statistical Analysis

Descriptive statistics are presented to summarize data from the registration CRF. Distribution of continuous variables was examined for normality. Because the assumption of normality is questioned, we performed the Kruskal–Wallis test followed by the Dunn procedure to test for differences in practices among world regions. The World was divided into six geographical regions: North America, Latin America (includes Mexico, Central and South America), Europe, Middle East and Africa, Asia, and Oceania. All *P* values were 2-tailed, with *P* < 0.05 deemed statistically significant. All statistical analyses were performed using SAS version 9.2.

Results

Investigators from 257 institutions located in 47 countries registered for participation (Appendix A in Supplementary material). The majority of participating institutions

were in the USA (115; 45%), followed by India (20; 8%), Spain (10; 4%), and Argentina (10; 4%). According to geographic location, 119 (46.3%) sites were in North America (115 in USA and 4 in Canada), 44 (17.2%) in Europe, 34 (13.3%) in Asia, 9 (3.5%) in the Middle East, 34 (13.3%) in Latin America, and 14 (5.5%) in Oceania.

At the time of the PRINCE Study launch, NCRN consisted of 170 sites from 23 countries. All NCRN sites registered for participation in the study (100% response rate). As indicated in the Study Design section, we also sent electronic invitations to members of the Neurointensive care section of the ESICM, LABIC, the Clinical Trials Group of the ANZICS-CTG, CCCTG, IGNITE of the German Neurointensive Care Society, the Chinese University of Hong Kong, and NCC-MENA chapter of the International Pan Arab Critical Care Medicine Society. ANZICS-CTG submitted the survey to 10 of their sites (100% response rate), and the Chinese University of Hong Kong to 1 site (100% response rate). Unfortunately, we did not keep track of the exact number of people who received the e-mail invitation for the other organizations, and as such are unable to provide these data.

Characteristics of Participating Institutions

The majority of participating sites were academic institutions (73.15%) located in large urban centers (43.92% in cities with >1 million inhabitants) regardless of geographic location (Table 1). The majority of respondents reported having a dedicated neuro-ICU (67.06%). However, most of them and the highest number of dedicated beds are located in North America (82.35%) with the lowest proportion in Oceania (14.29%). Pulmonary and Critical Care intensivists represent the highest proportion of practitioners caring for neurocritically ill patients in all World regions (37.65%) except North America where neurointensivists constitute the largest numbers (28.57%). The lowest proportion of neurointensivists is in Oceania (8.33%). Most institutions reported having neurology and neurosurgery residency (67.73% and 71.03%, respectively) and critical care fellowship training programs (72.22%). The number of neurocritical care fellowship training programs is much lower (27.38%) with the highest training opportunities available in North America (39.83%). The use of telemedicine is not widespread among study participants particularly in-house tele ICU (19.76%). The availability of telemedicine for remote hospitals is greater in those sites located in North America (63.56%).

Table 1 Characteristics of registered sites according to geographic location

	All	North America	Europe	Asia	Middle East	Latin America	Oceania	<i>p</i> value ^a
Type of institution: <i>n</i> (%)								
Academic	188 (73.15)	84 (70.59)	35 (79.55)	23 (67.65)	9 (100)	25 (67.57)	12 (85.71)	< 0.0001
Private non-academic	34 (13.23)	21 (17.65)	0 (0.00)	7 (20.59)	0 (0.00)	0 (0.00)	1 (7.14)	
Public non-academic	19 (7.39)	8 (6.72)	6 (13.64)	1 (2.94)	0 (0.00)	6 (13.64)	1 (7.14)	
Other	16 (6.23)	6 (5.04)	3 (6.82)	3 (8.82)	0 (0.00)	3 (6.82)	0 (0.00)	
City population: <i>n</i> (%)								
< 100K	11 (4.31)	8 (6.72)	1 (2.27)	2 (6.25)	0 (0.00)	0 (0.00)	0 (0.00)	0.0220
100K–250K	30 (11.76)	12 (10.08)	11 (25.00)	4 (12.50)	0 (0.00)	3 (8.11)	0 (0.00)	
251K–500K	38 (14.90)	17 (14.29)	8 (18.18)	3 (9.38)	1 (11.11)	8 (21.62)	1 (7.14)	
501K–750K	28 (10.98)	16 (13.45)	8 (18.18)	1 (3.13)	0 (0.00)	1 (2.70)	2 (14.29)	
751K–1m	36 (14.12)	21 (17.65)	6 (13.64)	4 (12.50)	0 (0.00)	3 (8.11)	2 (14.29)	
> 1m	112 (43.92)	45 (37.82)	10 (22.73)	18 (56.25)	8 (88.89)	22 (59.46)	9 (64.29)	
Dedicated neuro-ICU: <i>n</i> (%)								
Yes	171 (67.06)	98 (82.35)	29 (65.91)	19 (57.58)	3 (37.50)	20 (54.05)	2 (14.29)	< 0.0001
No	84 (32.94)	21 (17.65)	15 (34.09)	14 (42.42)	5 (62.50)	17 (45.95)	12 (85.71)	
Type of intensivist: <i>n</i> (%)								
Neurointensivist	17 (20.00)	6 (28.57)	2 (13.33)	3 (20.00)	1 (20.00)	4 (23.53)	1 (8.33)	0.0020
Pulmonary and critical care	32 (37.65)	4 (19.05)	5 (33.33)	3 (20.00)	3 (60.00)	10 (58.82)	7 (58.33)	
Anesthesiologist	14 (16.47)	0 (0.00)	7 (46.67)	6 (40.00)	0 (0.00)	1 (5.88)	0 (0.00)	
Surgery	4 (4.71)	4 (19.05)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	
Neurosurgery	3 (3.53)	2 (9.52)	0 (0.00)	1 (6.67)	0 (0.00)	0 (0.00)	0 (0.00)	
Other	15 (17.65)	5 (23.81)	1 (6.67)	2 (13.33)	1 (20.00)	2 (11.76)	4 (33.33)	
Neuro-ICU beds in hospital (median and range)								
	12 (0, 830)	16 (0, 830)	9 (0, 31)	10 (0, 35)	6 (0, 15)	6 (0, 18)	10 (0, 23)	< 0.0001
Number of ICU beds in hospital (median and range)								
	53 (0, 850)	78.5 (0, 850)	40 (8, 750)	39 (6, 400)	35 (12, 87)	20 (6, 800)	24 (19, 850)	< 0.0001
Neurology residency: <i>n</i> (%)								
Yes	170 (67.73)	79 (67.52)	38 (88.37)	19 (57.58)	6 (85.71)	15 (40.54)	13 (92.86)	< 0.0001
No	81 (32.27)	38 (32.48)	5 (11.63)	14 (42.42)	1 (14.29)	22 (59.46)	1 (7.14)	
Neurosurgery residency: <i>n</i> (%)								
Yes	179 (71.03)	71 (60.17)	38 (88.37)	24 (72.73)	6 (85.71)	26 (70.27)	14 (100.00)	< 0.0001
No	73 (28.97)	47 (39.83)	5 (11.63)	9 (27.27)	1 (14.29)	11 (29.73)	0 (0.00)	
Critical care fellowship: <i>n</i> (%)								
Yes	182 (72.22)	80 (67.80)	35 (81.40)	23 (69.70)	5 (71.43)	25 (67.57)	14 (100.00)	0.1153
No	70 (27.78)	38 (32.20)	8 (18.60)	10 (30.30)	2 (28.57)	12 (32.43)	0 (0.00)	
Neurocritical care fellowship: <i>n</i> (%)								
Yes	69 (27.38)	47 (39.83)	10 (23.26)	4 (12.12)	0 (0.00)	6 (16.22)	2 (14.29)	0.0015
No	183 (72.62)	71 (60.17)	33 (76.74)	29 (87.88)	7 (100.00)	31 (83.78)	12 (85.71)	
In-house tele-ICU: <i>n</i> (%)								
Yes	50 (19.76)	29 (24.37)	5 (11.63)	3 (9.09)	2 (28.57)	7 (18.92)	4 (28.57)	0.2358
No	203 (80.24)	90 (75.63)	38 (88.37)	30 (90.91)	5 (71.43)	30 (81.08)	10 (71.43)	
Telemedicine for remote hospitals: <i>n</i> (%)								
Yes	110 (43.82)	75 (63.56)	19 (45.24)	7 (21.21)	1 (14.29)	3 (8.11)	5 (35.71)	< 0.0001
No	141 (56.18)	43 (36.44)	23 (54.76)	26 (78.79)	6 (85.71)	34 (91.89)	9 (64.29)	

ICU intensive care unit

^a Kruskal–Wallis test followed by the Dunn procedure**Distribution of Resource Allocation**

There are several notable findings in resource allocation across the World regions (Table 2). Physician availability

24 h in ICU was the highest resource reported (87.75%) although it was lowest in North America (79.83%). Sites in Oceania reported the highest proportion of dedicated

Table 2 ICU characteristics according to resource allocation in the various world regions

	ALL	North America	Europe	Asia	Middle East	Latin America	Oceania	<i>p</i> value ^a
Physician available 24 h in ICU: <i>n</i> (%)								
Yes	222 (87.75)	95 (79.83)	42 (97.67)	31 (93.94)	7 (100.00)	34 (91.89)	13 (92.86)	0.0203
No	31 (12.25)	24 (20.17)	1 (2.33)	2 (6.06)	0 (0.00)	3 (8.11)	1 (7.14)	
Dedicated pharmacist: <i>n</i> (%)								
Yes	170 (68.00)	105 (88.98)	20 (47.62)	15 (45.45)	4 (66.67)	14 (37.84)	12 (85.71)	< 0.0001
No	80 (32.00)	13 (11.02)	22 (52.38)	18 (54.55)	2 (33.33)	23 (62.16)	2 (14.29)	
Dedicated physiotherapist: <i>n</i> (%)								
Yes	155 (61.75)	59 (50.43)	32 (74.42)	23 (69.70)	5 (71.43)	23 (62.16)	13 (92.86)	0.0064
No	96 (38.25)	58 (49.57)	11 (25.58)	10 (30.30)	2 (28.57)	14 (37.84)	1 (7.14)	
Dedicated respiratory therapist: <i>n</i> (%)								
Yes	164 (65.60)	101 (85.59)	11 (26.19)	14 (42.42)	6 (85.71)	31 (83.78)	1 (7.69)	< 0.0001
No	86 (34.40)	17 (14.41)	31 (73.81)	19 (57.58)	1 (14.29)	6 (16.22)	12 (92.31)	
Dedicated advanced practice providers: <i>n</i> (%)								
Yes	105 (42.00)	87 (73.73)	5 (11.90)	6 (18.18)	0 (0.00)	6 (16.22)	1 (7.69)	< 0.0001
No	145 (58.00)	31 (26.27)	37 (88.10)	27 (81.82)	7 (100.00)	31 (83.78)	12 (92.31)	
Daytime nursing/patient ratio: <i>n</i> (%)								
1:1	83 (32.30)	37 (31.09)	9 (20.45)	14 (41.18)	5 (55.56)	4 (10.81)	14 (100.00)	< 0.0001
1:2	173 (67.32)	105 (88.24)	30 (68.18)	18 (52.94)	3 (33.33)	16 (43.24)	1 (7.14)	< 0.0001
1:3	23 (8.95)	1 (0.84)	7 (15.91)	1 (2.94)	0 (0.00)	13 (35.14)	1 (7.14)	< 0.0001
1:4	5 (1.95)	0 (0.00)	1 (2.27)	1 (2.94)	0 (0.00)	3 (8.11)	0 (0.00)	0.0541
Other	4 (1.56)	1 (0.84)	1 (2.27)	0 (0.00)	0 (0.00)	2 (5.41)	0 (0.00)	0.3675
Nighttime nursing/patient ratio: <i>n</i> (%)								
1:1	70 (27.24)	34 (28.57)	6 (13.64)	8 (23.53)	5 (55.56)	3 (8.11)	14 (100.00)	< 0.0001
1:2	159 (61.87)	103 (86.55)	19 (43.18)	22 (64.71)	1 (11.11)	13 (35.14)	1 (7.14)	< 0.0001
1:3	38 (14.79)	6 (5.04)	16 (36.36)	3 (8.82)	1 (11.11)	11 (29.73)	1 (7.14)	< 0.0001
1:4	16 (6.23)	0 (0.00)	5 (11.36)	1 (2.94)	1 (11.11)	9 (24.32)	0 (0.00)	< 0.0001
Other	2 (0.78)	1 (0.84)	0 (0.00)	0 (0.00)	0 (0.00)	1 (2.70)	0 (0.00)	0.6216
Dedicated transport team: <i>n</i> (%)								
Yes	117 (46.61)	48 (41.03)	17 (39.53)	18 (54.55)	4 (57.14)	22 (59.46)	8 (57.14)	0.2557
No	134 (53.39)	69 (58.97)	26 (60.47)	15 (45.45)	3 (42.86)	15 (40.54)	6 (42.86)	
Portable CT scanner: <i>n</i> (%)								
Yes	43 (17.06)	37 (31.36)	3 (6.98)	1 (3.03)	1 (14.29)	1 (2.70)	0 (0.00)	< 0.0001
No	209 (82.94)	81 (68.64)	40 (93.02)	32 (96.97)	6 (85.71)	36 (97.30)	14 (100.00)	

CT computed tomography, ICU intensive care unit

^a Kruskal–Wallis test followed by the Dunn procedure

physiotherapists (92.86%) and nursing/patient ratio (100% 1:1). Availability of a dedicated respiratory therapist was higher in North America (85.59%), Middle East (85.71%) and Latin America (83.78%) and lowest in Oceania (7.69%). The availability of dedicated Advanced Practice Providers (APPs) is very high in the USA (73.37%) and very low in the other World regions (Europe 11.9%; Asia 18.18%; Middle East 0%; Latin America 16.22%; and Oceania 7.69%). The availability of dedicated pharmacists is higher in North America (USA and Canada) (88.98%) and Oceania (85.71%), compared to other World regions (Europe 47.62%; Asia 45.45%; Middle East 66.67%; and Latin America 37.84%). Overall, the use of portable

computed tomography scanners is uncommon (17.06%) but highest in North America (31.36%).

Use of Clinical Management Protocols

We found that the use of clinical management protocols also varies depending on the World region (Table 3). Institutions in Oceania and Asia were the least likely to report use of clinical management protocols. The most commonly used protocols were for venous thromboembolism prevention (75.49%), American Heart Association (AHA) acute ischemic stroke guidelines (72.76%), and ventilator-associated pneumonia prevention (73.54%). Overall, North American (USA and Canada) and Latin

Table 3 Type of clinical management protocol available in the ICU

	All	North America	Europe	Asia	Middle East	Latin America	Oceania	<i>p</i> value ^a
Type of protocol: Yes <i>n</i> (%)								
Acute ischemic stroke following AHA guidelines	187 (72.76)	111 (93.28)	16 (36.36)	20 (58.82)	6 (66.67)	31 (83.78)	3 (21.43)	< 0.0001
Acute ischemic stroke following European guidelines	36 (14.01)	5 (4.20)	24 (54.55)	2 (5.88)	1 (11.11)	3 (8.11)	1 (7.14)	< 0.0001
Subarachnoid hemorrhage following NCS guidelines	106 (41.25)	52 (43.70)	20 (45.45)	8 (23.53)	3 (33.33)	19 (51.35)	4 (28.57)	0.1711
Subarachnoid hemorrhage following AHA guidelines	123 (47.86)	68 (57.14)	16 (36.36)	12 (35.29)	4 (44.44)	18 (48.65)	5 (35.71)	0.0917
Intracerebral hemorrhage following the AHA guidelines	149 (57.98)	89 (74.79)	14 (31.82)	12 (35.29)	6 (66.67)	27 (72.97)	1 (7.14)	< 0.0001
Intracerebral hemorrhage following the European guidelines	33 (12.84)	4 (3.36)	24 (54.55)	1 (2.94)	1 (11.11)	2 (5.414)	1 (7.14)	< 0.0001
Status epilepticus following the NCS guidelines	117 (45.53)	55 (46.22)	24 (54.55)	11 (32.35)	4 (44.44)	20 (54.05)	3 (21.43)	0.1449
Mechanical ventilation sedation	178 (69.26)	84 (70.59)	30 (68.18)	22 (64.71)	6 (66.67)	30 (81.08)	6 (42.86)	0.1864
Mechanical ventilation weaning	175 (68.09)	86 (72.27)	28 (63.64)	20 (58.82)	7 (77.78)	30 (81.08)	4 (28.57)	0.0068
Sepsis following the Surviving Sepsis Campaign Guidelines	171 (66.54)	80 (67.23)	30 (68.18)	20 (58.82)	6 (66.67)	32 (86.49)	3 (21.43)	0.0011
Traumatic brain injury following the Brain Trauma Foundation Guidelines	157 (61.09)	70 (58.82)	31 (70.45)	15 (44.12)	4 (44.44)	30 (81.08)	7 (50.00)	0.0156
Induced hypothermia for comatose survivors of cardiac arrest	167 (64.98)	96 (80.67)	28 (63.64)	13 (38.24)	5 (55.56)	15 (40.54)	10 (71.43)	< 0.0001
Ventilator-associated pneumonia prevention	189 (73.54)	95 (79.83)	28 (63.64)	26 (76.47)	5 (55.56)	31 (83.78)	4 (28.57)	0.0004
Deep venous thrombosis prevention	194 (75.49)	94 (78.99)	32 (72.73)	24 (70.59)	7 (77.78)	27 (72.97)	10 (71.43)	0.8904
Osmolar therapy for cerebral edema and elevated intracranial pressure	151 (58.75)	71 (59.66)	33 (75.00)	15 (44.12)	3 (33.33)	23 (62.16)	6 (42.86)	0.0365
Fever management	132 (51.36)	74 (62.18)	22 (50.00)	13 (38.24)	2 (22.22)	16 (43.24)	5 (35.71)	0.0202
Systemic anticoagulation	150 (58.37)	78 (65.55)	28 (63.64)	11 (32.35)	5 (55.56)	20 (54.05)	8 (57.14)	0.0252
Elevated intracranial pressure management	164 (63.81)	72 (60.50)	34 (77.27)	18 (52.94)	5 (55.56)	26 (70.27)	9 (64.29)	0.2446
External ventricular drain management and weaning	118 (45.91)	52 (43.70)	25 (56.82)	12 (35.29)	5 (55.56)	14 (37.84)	10 (71.43)	0.1146

AHA American Heart Association, ICU intensive care unit, NCS Neurocritical Care Society

^a Kruskal–Wallis test followed by the Dunn procedure

American sites had most similarity in the types of protocols used particularly for management of acute ischemic stroke (93.28% and 83.78%, respectively, for AHA protocol), intracranial (74.79% and 72.97%, respectively, for AHA protocol) and subarachnoid hemorrhage (43.7% and 51.35% for NCS protocol), status epilepticus (46.42% and 54.05% for NCS protocol), and osmolar therapy for cerebral edema and elevated intracranial pressure (ICP) (59.66% and 62.16%, respectively). Sites in Oceania and North America reported the highest proportion of use of induced hypothermia for comatose survivors of cardiac arrest (80.67% and 71.43%, respectively), whereas European and Latin American sites reported the highest proportion of use of protocols for ICP management (77.27% and 70.27%, respectively).

Discussion

The PRINCE Study represents the first international multicenter study to evaluate the scope of practice of neurocritical care. Our findings suggest that there is worldwide variability in the manner neurocritical care is delivered. In addition, we have shown the feasibility of undertaking international collaborations to start filling the gaps left by the dearth of global epidemiological data related to general and neurocritical care [14–17].

Strengths and Limitations

The PRINCE Study has several strengths. The data were collected prospectively. Participating investigators received education and training related to study aims and data collection before study initiation. Participating

institutions were distributed throughout the World except Africa. However, the PRINCE Study also has several limitations. First, participation was voluntary and uncompensated. It is possible that these may have affected the number of participating institutions. Therefore, the information provided may not represent the true worldwide delivery of neurocritical care but rather the care delivered at the participating institutions. Second, the majority of sites comprised of large academic institutions located in major cities. Generalizability of the results is limited since we cannot infer the manner neurocritical care is practiced in other hospital settings. Third, data collection was not monitored. We only monitored and verified incongruous data and outliers. Fourth, the sample size was determined by the number of sites and investigators that volunteered to participate and not by statistical calculations. Therefore, it is possible that the PRINCE Study is underpowered to detect meaningful statistical differences in several of the variables collected. Despite all these limitations, it is worth noting that the results of the PRINCE Study align in several ways with those from earlier work on neurocritical care using administrative datasets [18], supporting the generalizability of the data presented.

Implications of the PRINCE Study and Future Direction

The PRINCE Study prospectively collected data from international sites, which provides an important insight into the global organization of neurocritical care delivery worldwide. However, the data collected raise several points that need to be clarified in subsequent prospective observational studies. Participation of a larger number of non-academic institutions located in cities of diverse sizes and from a larger number of countries including Africa will be needed to be able to have a broader view of available models of neurocritical care delivery. More detailed data on daily activities in the ICU where neurocritical care is delivered is needed to be able to ascertain educational needs in this field and adjust them according to local practices and availability of resources. The role of various practitioners working in those ICUs also needs to be delineated along with the types of interactions that take place among those who work in NCCUs. For example, the role of APPs including the type of work they perform and the hours they spend in the NCCU deserves more attention in future observational studies. All these points are of critical importance since most neurocritically ill patients are cared for in mixed-type ICUs rather than dedicated neuro-ICUs. Lastly, healthcare expenditures associated with staffing of ICUs need to be collected to understand how and where to allocate resources.

Conclusion

The PRINCE Study represents the first international collaboration designed to provide a snapshot of how neurocritically ill patients are cared for. The study results suggest that there is significant variability in the delivery of such care.

Electronic supplementary material

The online version of this article (<https://doi.org/10.1007/s12028-019-00750-3>) contains supplementary material, which is available to authorized users.

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Authors' contributions

JIS protocol development, data collection, data analysis, and manuscript writing/editing; RHM data collection, data management, data analysis, and manuscript writing/editing; CB data collection, data management, data analysis, and manuscript writing/editing; Alexandros Georgiadis: protocol development, data collection, data analysis, and manuscript writing/editing; Chethan P. Venkatasubba Rao: protocol development, data collection, data analysis, and manuscript writing/editing; EC protocol development, data collection, data analysis, and manuscript writing/editing; JCH protocol development, data collection, data analysis, and manuscript writing/editing; MO protocol development, and manuscript writing/editing; FST protocol development, and manuscript writing/editing; PDL protocol development, and manuscript writing/editing. The corresponding author confirms that authorship requirements have been met, the final manuscript was approved by ALL authors, and that this manuscript has not been published elsewhere and is not under consideration by another journal. There was no support for this work. The PRINCE Study adhered to ethical guidelines and the IRB at the Baylor College of Medicine approved it with a waiver of consent. We used the STROBE reporting checklist for observational studies.

Conflict of interest

Dr Suarez reports being President of the Neurocritical Care Society, a member of the Editorial Board of Stroke Journal, and Chair of the DSMB for the INTREPID Study sponsored by BARD, outside of the submitted work. Dr LeRoux has nothing to disclose. Dr Bauza has nothing to disclose. Dr Sung has nothing to disclose. Dr Hemphill has nothing to disclose. Dr Oddo has nothing to disclose. Dr Martin has nothing to disclose. Dr Taccone has nothing to disclose. Dr Georgiadis has nothing to disclose. Dr Venkatasubba Rao has nothing to disclose. Ms Calvillo has nothing to disclose.

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