neurocritical care society Neurocrit Care (2011) 14:291–317
DOI 10.1007/s12028-010-9453-z

REVIEW ARTICLE

Intracerebral Hemorrhage Specific Intensity of Care Quality Metrics

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Published online: 16 November 2010

Abstract
Background Intracerebral hemorrhage (ICH) care can vary among centers and previous studies have demonstrated differences in ICH outcome based on variations in patient care in various settings. The purpose of this paper is to present the design of an evidence-based dataset of elements of a new ICH specific intensity of care quality metrics.
Methods The articles were identified based on personal knowledge of the subject supplemented by data derived from multi-center randomized trials, and selected non-randomized or observational clinical studies. The information was identified with multiple searches on MEDLINE from 1986 through 2009. The current guidelines from American Heart Association (AHA)/American Stroke Association (ASA) Stroke Council and The European Stroke Initiative (EUSI) Writing Committee for management of ICH were reviewed extensively for identifying quality indicators and available scientific evidence. For certain elements where stroke-specific data was not available, data derived from other disease process with direct relevance was used.
Results A total of 26 quality indicators related to 18 facets of care with thresholds for quality response were identified. A pilot study was performed to asses and score 1300 (26 indicator per patientX25 patientsX2 raters) quality indicators. The minimum proportion of patients meeting quality parameter ranged from 44% to 100% depending upon the variable. The lowest performance scores were observed in the early intubation and mechanical ventilation, treatment of significant intracranial mass effect or transtentorial herniation, and timely acquisition of neuroimaging. The highest performance scores were seen in treatment of any seizure within 2 weeks of admission, status epilepticus, and prevention of gastric ulcer.
Conclusions The next step in development of a new ICH specific intensity of care quality metrics is validation and refinement of the quality indicators and thresholds presented in the current report. Future activities may include selection and validation based on consensus of experts and application of the system to a large series of patients with ICH and assessment of relationship of components in isolation and as a group to outcome after severity adjustment.

Keywords Intracerebral hemorrhage · Quality indicators · Intensity of care · Intensive care unit · Cerebral hemorrhage

Introduction

Intracerebral hemorrhage (ICH) care can vary among centers and previous studies have demonstrated differences in ICH outcome based on variations in patient care in various settings [1, 2]. A United States national analysis [2] demonstrated a shift in the frequency of hospital admissions for ICH to urban teaching hospitals, progressing from 30% in 1990–1991 to 49% in 2000–2001. There was a prominent reduction in mortality among admissions in urban teaching hospitals (relative reduction of 9%) that was not observed in urban non-teaching and rural hospitals (relative reduction of 2%) suggesting that both practice and application of new beneficial interventions may be different between hospitals. Diringer et al. [1] performed an analysis of data

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prospectively collected by Project Impact over 3 years from 42 participating intensive care units (ICUs) including one neuro ICU. The records of 36,986 patients were merged with records of 3,298 patients from a second neuro ICU that collected the same data over the same period. Multivariate analysis indicated that not being in a neuro ICU was associated with an increase in hospital mortality rate (odds ratio of 3.4) after adjustment for patient demographics, severity of ICH, and ICU and institutional characteristics. The benefit may be related to different approaches to management of blood pressure (BP), withdrawal of care, correction of coagulopathy, experience of caregivers, management of comorbidities, complications, and general supportive care. Conversely, implementation of relatively consistent approach to the diagnosis and care of the acute stroke patient using pre-defined standing orders and critical path care plan in a community hospital decreased length of stay and hospitalization costs of Medicare patients [3]. Introduction of a neurocritical care team, including a full-time neurointensivist with implementation of available protocols for patient care including care of the mechanically ventilated patient, deep venous thrombosis (DVT) and gastrointestinal prophylaxis, infection control, use of sedatives, blood glucose, core body temperature, and BP control was associated with significantly reduced in-hospital mortality and length of stay without changes in readmission rates or long-term mortality in a study based on one neuro ICU [4]. A review of 31 trials, involving 6,936 participants, compared stroke unit care with an alternative service [5]. The analysis demonstrated that a more organized care was consistently associated with improved outcomes. Stroke patients who receive organized inpatient care in a stroke unit are more likely to be alive, independent, and living at home 1 year after the stroke.

The intensity and variation of care can also impact upon results of clinical trials outcomes. Previous large, randomized trials [6, 7] have found differences in care patterns among sites that may impact the eventual study results. In the National Acute Brain Injury Study—Hypothermia [6] significant differences in intercenter outcomes of hypothermia-treated patients were observed, possibly related to significant differences in the incidence of mean arterial pressure <70 mmHg and cerebral perfusion pressure (CPP) <50 mmHg among patients in the various centers. The frequency of vasopressor use and morphine dose and percentage of dehydrated patients varied significantly among centers. Participation of small centers increased intercenter variance and diminished the quality of data. The investigators recommended continuous monitoring of protocol compliance and a run-in period for new centers to test accrual and protocol adherence. Subsequently, the National Institutes of Health (NIH) workshop on clinical trials in traumatic brain injury (TBI) [8] recommended frequent independent monitoring of patient management and data quality for future trials.

There is a need for an algorithm that evaluates principles of care using the "best available" evidence in a semi-quantitative manner to detect differences in intensity of care and eventually guide uniformity of care across sites. The purpose of the current effort was a first step towards standardization of medical care. The pertinent literature was reviewed to identify potential indicators of quality indicator for acute ICH care and subsequently test the feasibility and interobserver variability of the selected indicators.

Methods

The articles were identified based on personal knowledge of the subject supplemented by data derived from multi-center randomized trials, and selected non-randomized or observational clinical studies. The information was identified with multiple searches on MEDLINE from January 1st, 1986 through December 31st, 2009 by cross referencing key words of cerebral hemorrhage, intracerebral hemorrhage, neuroimaging, clinical studies, randomized trials, cytotoxicity, edema, hemostatic treatment, factor VII, acute hypertension, and oral anticoagulants. Other pertinent articles were identified through review of bibliography from selected articles. The abstracts from pertinent scientific meetings were also reviewed. The current guidelines from American Heart Association (AHA)/American Stroke Association (ASA) Stroke Council and The European Stroke Initiative (EUSI) Writing Committee for management of ICH were reviewed extensively for identifying quality indicators and available scientific evidence [9, 10]. The elements and scientific basis of management algorithm for patients with ICH presented in a recent article in Lancet [11] were also reviewed. For certain elements where stroke-specific data was not available, data derived from other disease process with direct relevance was used. Such data was sought after extensive literature search identified the prognostic value of the care aspect but was unable to identify stroke specific treatment paradigms (Table 1).

Rationale of Selection of Quality Indicator

Category 1: Emergency Department (ED) Evaluation

The time to initial evaluation for physician contact and hemodynamic monitoring (<10 min for both) has been recommended and used as a quality parameter in previous studies and is associated with more expedient acquisition of neuroimaging. For a primary stroke center, such protocols should include the emergency care of patients with ischemic stroke and hemorrhagic stroke, including stabilization of

Table 1 Description of variables selected for the intracerebral hemorrhage specific intensity of care quality metrics

Variables	Definition	Time to initiate[a]	Time to achieve therapeutic goal[c]	Sustained intervention/ monitoring[a]	Prevention of adverse event[c]	Characteristics of treatment
ED evaluation time	Time to physician contact and hemodynamic monitoring	<10 min Observational study (ies) (stroke specific)				
Expedient acquisition of neuroimaging	Time interval between ED arrival and CT scan or MRI	<25 min Care parameter NINDS rt-PA and ATACH (ICH specific) trials				
ICU monitoring[b]	Neurological and hemodynamic monitoring <30 min interval	<10 min Prospective trial (s) (ICH specific)				
Avoidance of do-not-resuscitate (DNR) or withdrawal of care status in first 24 h and DNR without cause within first 7 days	Appropriate causes include severe stroke, life-threatening brain damage, and significant comorbidities			Within 24 h Observational study (ies) (ICH specific) Within 7 days without cause Observational study (ies) (stroke specific)		
Management of acute hypertensive response	SBP ≥180 mmHg		<2.5 h Clinical trials (ICH specific)			
Early intubation and mechanical ventilation	Indications: decreased level of consciousness (GCS <10); hypoventilation or apnea or decreased or ineffective respiratory effort; hypoxemia or hypercarbia; impaired airway protection; airway obstruction; recurrent aspiration; seizures >5 min; or craniotomy.	<30 min Observational study (ies) (ICH specific)				
Treatment of clinically significant intracranial mass effect or transtentorial herniation	Unilateral or bilateral pupillary enlargement or two spontaneous ICP elevation >20 mmHg persisting for >5 min (if ICP monitoring is available		<1 h Observational study (ies) (stroke specific)		<7 days Observational study (ies) (stroke specific)	
Treatment of repetitive seizures and status epilepticus	Continuous or repeated seizure activity >5 min without recovery of consciousness		<20 min Randomized clinical trial (s) (status epilepticus specific)		<12 h Randomized clinical trial (s) (status epilepticus specific)	
Rapid reversal of elevated INR	INR >1.4 at admission		<2 h Observational study (ies) (ICH specific)			≥2 agents Observational study (ies) (ICH specific)

Table 1 continued

Variables	Definition	Time to initiate[a]	Time to achieve therapeutic goal[c]	Sustained intervention/ monitoring[a]	Prevention of adverse event[c]	Characteristics of treatment
Treatment of elevated serum glucose concentration	>200 mg/dl within 72 h		<4 h Observational study (ies) (ICH specific)		<72 h Observational study (ies) (ICH specific)	
Treatment of hyperpyrexia	$T \geq 38.3$°C on two consecutive measurements 1 h apart within 72 h		<4 h Randomized clinical trial (s) (neuro-ICU specific)		<72 h Randomized clinical trial (s) (neuro-ICU specific)	
DVT prophylaxis	Low molecular weight heparin, heparin, or IPC	<48 h Randomized clinical trial (s) (ICH specific)				
Dysphagia screening	Bedside evaluations, videofluoroscopic assessment, or fiberoptic endoscopy	<72 h Observational study (ies) (stroke specific)				
Feeding (nutrition) initiation	Enteric route preferred	<72 h Randomized trial (s) (stroke specific)				
Gastric ulcer prophylaxis	H2 blockers, proton blockers, or sucralfate	<48 h Randomized clinical trial (s) (ICH specific)				
Treatment of persistently elevated BP	SBP ≥160 mmHg) within 7 days	<7 days Randomized clinical trial (s) (stroke specific)				
Tracheostomy for persistent intubation, or poor airway protection	Early percutaneous or surgical tracheostomy	<7 days Randomized clinical trial (s) (mechanically ventilated pts specific)				
Treatment of hospital acquired or ventilator associated pneumonia	New or progressive radiographic infiltrate and at least two: fever, leukocytosis, or purulent tracheal secretions, during ICU stay	<24 h Observational study (ies) (VAP specific)				<10 days Observational study (ies) (VAP specific)

Abbreviations used: *ICH* intracerebral hemorrhage, *ICU* intensive care unit, *ED* emergency department, *SBP* systolic blood pressure, *ATACH* antihypertensive treatment of cerebral hemorrhage, *VAP* ventilator associated pneumonia, *DVT* deep venous thrombosis, *IPC* intermittent pneumatic compression, *INR* international normalized ratio, *ICP* intracranial pressure, *rt-PA* recombinant tissue plasminogen activator, *BP* blood pressure

[a] Time from arrival to ED

[b] Overlaps with Category #1

[c] Time from occurrence of event of interest

vital functions, initial diagnostic tests, and use of medications (including but not limited to intravenous (IV) recombinant tissue plasminogen activator [rt-PA] treatment) [12]. An organized protocol for the emergency evaluation of patients with suspected stroke is recommended (Class I, Level of Evidence [LOE] B) [13]. The NINDS rt-PA Stroke Trial required the ED or triage nurse performed laboratory studies, obtained baseline vital signs, and started an IV line (0.45 or 0.9 normal saline) within 5–10 min of the patient's arrival [14]. Quality indices denoting the emergency evaluation and treatment of patients with suspected stroke was considered a key element in the Centers for Disease Control and Prevention (CDC) national Paul Coverdell acute stroke registry to track and improve the delivery of care to stroke patients [15].

Time from ED arrival to ED physician evaluation was considered a quality indicator because it has been ascertained in previous studies. The mean time for evaluation among 630,402 estimated stroke patients were seen at EDs in 2003 was 30 ± 37 min, 34 ± 44 min, and 55 ± 105 min for those arriving by ambulance, walk-in, and public services/unknown mode of arrival, respectively [16]. While no definitive time criterion exists, door to physician time within 10 min of arrival was used as a quality parameter in the statewide, 16 hospital-based, Michigan Acute Stroke Care Overview and Treatment Surveillance System [17] and within 15 min was used as a variable in Neuroimaging In Stroke and Seizure As Neurological emergencies (NISSAN) study [18]. Among the 1,837 patients in the survey, 176 (10%) had a door to physician time within 10 min of arrival and therefore represented an area of improvement. Both studies [17, 18] reported an association between earlier physician evaluation and early neuroimaging. The National Symposium on Rapid Identification and Treatment of Acute Stroke recommended an initial patient evaluation (did not specify by physician) within 10 min of arrival [19].

The time requirements for ED physician evaluation are similar to those identified by American College of Cardiology (ACC)/AHA guidelines for management of patients with ST-elevation myocardial infarction (MI) which state that "a 12-lead ECG should be performed and shown to an experienced ED physician within 10 min of ED arrival for all patients with chest discomfort (or anginal equivalent) or other symptoms suggestive of STEMI (LOE: C)" [17].

Category 2: Expedient Acquisition of Neuroimaging

The time interval between ED arrival and acquisition of neuroimaging (<25 min) is consistent with the recommendations of National Symposium on Rapid Identification and Treatment of Acute Stroke that recommended initiating a CT scan within 25 min and interpreting the CT scan within 45 min of arrival [19]. The Brain Attack Coalition (BAC) [14, 15] recommendation differ slightly because it states that primary stroke centers must have the capability of performing either a CT scan or a brain magnetic resonance imaging scan within 25 min of the order being written and interpretation within 20 min of completion [12]. In a city wide study of 446 patients with suspected acute stroke, time interval between arrival and CT scan was one of the differentiating parameters between stroke centers and other hospitals [20]. In addition to the decision regarding IV rt-PA, different strategies are required for managing the acute hypertensive response in different subtypes of stroke [21]. The AHA/ASA Stroke Council state that "ICH is a medical emergency, with frequent early, ongoing bleeding and progressive deterioration, severe clinical deficits, and subsequent high mortality and morbidity rates, and it should be promptly recognized and diagnosed (Class I, LOE A)" [9].

This quality indicator has been consistently evaluated in previous studies. A audit found that among the 3,795 patients who arrived at the ED within 2 h of symptom onset, 3,491 had data recorded regarding the interval from ED arrival to receipt of brain imaging [22]. A total of 2,275 (65.2%) received imaging within 1 h of ED arrival. A higher proportion of patients transported by emergency medical services (EMS) received imaging within 1 h compared with non EMS transported patients. Among those patients who arrived at the ED within 2 h, the median time from ED arrival to brain imaging was 0.73 h (43.8 min). In the Genentech Stroke Presentation Survey [23], the median time from ED arrival until CT scan completion was 1.1 (0.7–1.8) h among 1,207 patients with stroke symptoms presenting to 48 EDs. Patients who arrived by EMS had significantly shorter pre-hospital delay times and times to CT scan. Time interval between ED arrival and CT scan was an important modifiable determinant of delay time for the treatment of acute strokes in this large geographically diverse study. A review of 123 studies [24] published from 1981 to 2007 of pre-hospital and in-hospital delay time for evaluation and treatment of patients with stroke demonstrated a 10.7% annual decline in hours/year for delay time from ED arrival to initiation of CT scan ($P = 0.11$ based on 23 population groups). A review of 479,284 consecutive stroke and TIA admissions at 905 hospitals suggested that ICH patients were more likely to undergo CT scan within 25 min of arrival compared with ischemic stroke and TIA patients; 40% vs. 30% of admissions [25]. ICH patients had more rapid improvement per year in door-to-CT time.

Although deferred until therapies that require use of thrombolytics in ICH are considered standard of care, serial CT scans to document stability of hematoma maybe used as a quality parameter. Initial and repeat CT scan 6 h apart has been used in Clot Lysis Evaluating Accelerated

Resolution of IntraVentricular Hemorrhage (CLEAR-IVH) [26] and Minimally Invasive Surgery plus t-PA for Intracerebral hemorrhage Evacuation (http://clinicaltrials.gov/ct2/show/NCT00224770) to document stability of ICH prior to recruitment in patients presenting within 12 h of symptom onset.

Category 3: ICU Monitoring

The quality parameter requiring admission to dedicated ICU for at least 24 h after the clinical event is consistent with all current recommendations due to the high risk of neurologic deterioration, cardiovascular instability, and need for intubation during the first 24 h after the onset of an ICH [9, 11, 27]. The AHA/ASA Stroke Council state that "monitoring and management of patients with an ICH should take place in an ICU setting because of the acuity of the condition, frequent elevations in intracranial pressure (ICP) and BP, frequent need for intubation and assisted ventilation, and multiple complicating medical issues" [9]. In one study of 1,038 ICH patients admitted to the ICU [1], medical reasons including impaired consciousness, elevated BP, and frequent need for intubation were cited as the reasons for admission in 83% of the 1,038 patients. Hourly assessment of neurological status with use of a standard evaluation such as Glasgow Coma Scale (GCS) score is necessary for detection of deterioration. In a study of 95 patients presented with an initial GCS score >12, 22 (23%) had early deterioration [28]. The mean time from presentation to early deterioration was 8 h. A cohort study conducted in 266 patients with supratentorial ICH admitted consecutively to 15 hospitals within 12 h of symptom onset [29] found that early neurological deterioration occurred in 61 patients (23%) within 48 h of admission. The Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) [30] prospectively ascertained the rate of neurological deterioration in 60 patients with ICH with elevated SBP $\geq$170 mmHg who presented to the ED within 6 h of symptom onset. A total of seven neurological deteriorations were detected ranging from 5 min to 19 h after recruitment and initiation of antihypertensive treatment.

Frequent BP monitoring has been recommended in previous studies such as ATACH I [6] assessing systemic BP changes in patients with ICH. A minimum of two measurements at 30 min interval per hour was recommended, based on ATACH I trial protocol [6], to define regular monitoring. The recommendation is made with the understanding that measurements usually range from every 5 min to15 min if IV antihypertensive medication is being initiated or dose is adjusted and subsequently every 15–30 min for duration of infusions. More frequent measurements maybe necessary if prominent BP changes are observed as determined by the treating physician. Intra-arterial BP monitoring was not selected as a quality parameter because BP can be adequately monitored with an automated cuff [31, 32]. Cardiovascular instability in association with increased ICP needs immediate attention to avoid the deleterious effects of hypertension or hypotension in a patient with limited autoregulatory capacity. In a study of 105 patients, the slope of mean arterial pressure (faster rate of decline) within the first 24 h was independently associated with increased mortality in patients with ICH particularly those with lower initial BP [33]. Additional issues regarding hemodynamic monitoring and BP management are described in detail in the next section.

Category 4: Avoidance of Do-Not-Resuscitate (DNR) or Withdrawal of Care Status

The quality parameters were recommended to avoid limiting care for ICH patients who may survive their acute illness and reduce the impact of physician beliefs. Early care limitations are independently associated with both short- and long-term all-cause mortality after ICH despite adjustment for expected predictors of ICH mortality [34]. Variations in the use of DNR was reported in 7,265 all-cause ICU admissions at 13 hospitals ranging from 0.4% to 14%, and the mean interval from ICU admission to DNR order ranged from 5.4 to 24 days [35]. These variations could not be explained by differences in patient characteristics, and were attributed to various physician attitudes. In another study of 1,719 patients admitted to the two ICUs with any cause [36], life support was withheld from 1% and withdrawn from 5% of the patients. Withdrawal of care decisions preceded about half of all deaths that occurred within the two ICUs surveyed [36]. A review of 1,421 patients with ICH demonstrated that care limitations or withdrawal of life-sustaining interventions was the most common (in 68%) cause of death [37]. Becker et al. [38] reported that 23 of the 30 deaths in 87 patients with ICH were related to withdrawal of care. In the multivariate model, the most important prognostic variable in determining outcome after ICH was withdrawal of support. A concomitant survey by Becker et al. [38] conducted among 31 members of the departments of neurology and neurologic surgery suggested that most physicians rely upon the volume of ICH >60 cc and the GCS <8 to recommend withdrawal of care. However, this perspective was considered to reduce the opportunity of recovery in a subset of patients who achieved functional independence in actuality despite meeting the ICH volume and GCS criteria for futility.

The American College of Chest Physicians/Society of Critical Care Medicine Consensus Panel [39] recommended that if there is reasonable medical certainty of nonsalvageable condition, intensive measures should not be undertaken. However, there may be religious or expressed

patient and family reasons which could justify initiation of intensive care with the understanding that futile intervention is a temporary measure. In acute settings, medical professionals may not know all the necessary information and panel favored treatment until all the relevant facts are known. Reliance on objective data only available at the time of presentation is frequently insufficient to preclude withdrawal of care. The panel recommended that decision making should be based on combination of objective prognostic data and personal patient preferences and values.

4A. DNR Status Within 24 h of Admission

Withdrawal of care within 24 h of admission was considered premature and an adverse parameter. The recommendation is based on the assumption that such a criterion will not always be applicable due to previous living will precluding aggressive medical care or DNR. The intention is to avoid excessive use of early withdrawal of care which correlates with higher risk-adjusted mortality. A review of all 8,233 ICH admissions treated in 234 hospitals to nonfederal hospitals in California during 1999 and 2000 reported that proportion of patients with DNR orders within the first 24 h of hospitalization varied from 0% to 70% across hospitals [40]. Mortality rate was shown to increase progressively for patients treated in quartiles of increasing patient characteristic adjusted hospital DNR use. Patients in the lowest quartile hospitals were more likely to be mechanically ventilated and more likely to undergo craniotomy, ventriculostomy, or cerebral angiography. Admission to a hospital that used DNR orders 10% more often than another hospital with a similar case mix increased a patient's odds of in-hospital deaths by 13%. Zahuranec et al. [41] reviewed 270 ICH cases in the Brain Attack Surveillance in Corpus Christi (BASIC) project. Early ($<$24 h from presentation) DNR orders or withdrawal of care was documented in 34% of cases and was associated with a two-fold higher hazard of death both at 30 days (hazard ratio [HR] 2.2) and at end of follow-up (HR 1.9) after adjustment for important confounders including age, GCS, ICH volume, and intraventricular hemorrhage.

4B. DNR Status Between 24 h and 7 days of Admission without Documentation of Appropriate Justification

Withdrawal of care between 24 h and 7 days of admission without documentation of appropriate justification was also considered an adverse parameter. Alexandrov et al. [42] reported that DNR status was used to 31% of all 450 consecutive patients with acute hemispheric strokes (36 patients had ICH) at some time during their admission. Fifty-three percent of DNR orders were given within first 24 h of the hospital stay, 35% during the first week of the hospital stay, and 12% at any time between days 8 and 44. While the overall mortality in the study was 26%, 83% of those with a DNR status died. Subsequently, a multicenter evaluation of the provisional criteria among physicians of the Canadian and Western New York Stroke Consortiums highlighted the importance of disease-specific criteria for DNR status [43]. An agreement was reached that DNR decision is appropriate when any two of the following three clinical criteria are present: severe stroke; life-threatening brain damage; and significant comorbidities. The definitions were as follows: clinically severe stroke was defined by persisting (more than 24 h) and sometimes deteriorating neurological deficit, including little or no active movement on at least one side of the body, with impaired consciousness, global aphasia, or lack of response indicating cognition. Life-threatening brain damage was defined by brain stem compression caused by large ICH, usually with intraventricular extension. Significant co-morbidity was defined by pneumonia, pulmonary embolism, sepsis, recent myocardial infarction, cardiomyopathy, and life-threatening arrhythmias.

Category 5: Treatment of Acute Hypertensive Response

Intravenous (IV) antihypertensive medication titrated to effect for 24 h after ED arrival for elevated BP (SBP $\geq$180 mmHg) in patients with ICH was selected as a quality parameter based on high prevalence and guidelines from professional organizations. In an analysis of 45,330 patients with ICH, 75% had SBP $>$140 mmHg and 20% had SBP $>$180 mmHg at presentation [44]. The current ASA/AHA [9] and EUSI [10] guidelines recommend lowering of BP in patients with an ICH to maintain SBP $<$180 mmHg. An initial SBP of $\geq$200 mmHg is associated with hematoma expansion [45] and increased mortality [46] among patients with ICH. Persistently higher SBP is also associated with perihematoma brain edema formation [47]. Reducing BP may reduce the rate of hematoma expansion although conclusive evidence is not available [48, 49]. Recent studies suggest that reduction of BP may be tolerated because of reduced metabolism (hibernation) [50] and preserved autoregulation in the perihematoma region [51].

5A. The Therapeutic Target

The target SBP $\geq$180 mmHg for initiating treatment was based on AHA/ASA Stroke Council [9] and EUSI [10] guidelines. The tolerability of current AHA guideline based treatment was observed in 25 of the 29 (86%) patients in one study [52]. Neurologic deterioration and hematoma enlargement was observed in four and five of 29 patients, respectively. The agents that are recommended by the ASA

for the acute hypertensive response are either IV or transdermal agents with rapid onset and short duration of action to allow precise titration [21]. Indirect comparisons suggest that IV bolus regimens of antihypertensive agents have higher variability in BP control than infusion regimens [52]. Both ASA/AHA [9] and EUSI [10] guidelines acknowledge that there may be a subset of patients who can tolerate more aggressive BP reduction but there is continued concern that lowering CPP could precipitate ischemic damage [33]. The ATACH [30] and another randomized pilot study, Intensive BP Reduction in Acute Cerebral Haemorrhage (INTERACT) [48], recently reported that aggressive BP reduction to a target of <140 mmHg within 6 h of symptom onset probably decreases the rate of substantial hematoma enlargement [48] without increasing adverse events [30]. However, the effect on clinical outcome has not yet been fully evaluated and therefore, the more conservative targets that were set in the ASA and EUSI guidelines should be followed [11].

5B. Use of SBP to Guide Treatment (Adjunct to Quality Indicator)

SBP was used to define treatment target because the present evidence supports the association between SBP and hematoma expansion [45, 53]. Previous studies identified elevated SBP as a risk factor for hematoma expansion with no clear relationship with DBP. Both ATACH I [30] and INTERACT [48] used treatment goals defined by SBP to determine safety, and INTERACT demonstrated attenuation of hematoma expansion with SBP reduction. Furthermore, Morfis et al. [54] observed that SBP in patients with ICH shows large fluctuations and variability with a loss of normal diurnal rhythm using 24-h ambulatory BP monitoring on day 1. Changes were less prominent in DBP. Since MAP is more a reflection of DBP, it may underestimate dynamic changes of BP in the first 24 h of ICH. We chose an infusion to be up to 24 h after initiation of treatment (24–27 h after symptom onset), to provide adequate SBP control during the time that hematoma expansion will mostly occur. Although the rate of hematoma expansion is highest in the first 3 h after symptom onset [53, 55], expansion occurs in 12–37% of patients between 3 and 24 h after symptom onset. Early termination of antihypertensive treatment may lead to poor control of SBP, with subsequent increase in delayed bleeding. Hematoma expansion after the first 24 h was evaluated in two studies and found to be rare [53, 56].

5C. Time to Achieve Target

Treatment success was defined if target BP range was achieved within 2.5 h of elevated BP detection (based on time interval between two consecutive SBP $\geq$180 mmHg and first SBP $<$180 mmHg recordings). Actual lowering of SBP and not the treatment goal specified was associated with lower rates of hematoma expansion and death and disability at 3 months in the ATACH I study [49]. The same endpoint was used in the ATACH study where treatment success was defined by SBP reduction and maintenance in the respective target range [30]. Treatment failure was defined as the observed hourly minimum SBP remaining greater than the upper limit of the target range for 2 consecutive hours after initiation of nicardipine infusion. A time limit of 2.5 h accounts for 30 min to initiate treatment [57]. Treatment failure was ascertained by study statistician at statistical and data management center after review of hourly maximum and minimum SBP recordings. Of those screened, 60 patients were enrolled with 18, 20, and 22 patients recruited in tier 1 (SBP $\geq$170 mmHg and $<$200 mmHg), tier 2 (SBP $\geq$140 mmHg and $<$170 mmHg), and tier 3 (SBP $\geq$110 mmHg and $<$140 mm), respectively. Primary treatment failure was observed in 9 of 60 subjects, all in the last tier.

Category 6: Early Intubation and Mechanical Ventilation

Time interval between time of GCS score <8 documentation or other indications summarized in Table 2 and time of intubation was selected as a quality indicator based on the high proportion of patients who will require intubation and to avoid unnecessary delays in protecting the airway. Approximately 30% of patients with a supratentorial ICH and almost all patients with a brain-stem or cerebellar

Table 2 Indications of emergent intubation among patients with intracerebral hemorrhage

Decreased level of consciousness (Glasgow Coma Scale score <10)
Combination of no (or very brief) eye opening to noxious stimuli, failure to follow commands, or Glasgow Coma Scale score ≤8
Hypoventilation or apnea ($PCO_2 > 50$ mmHg) or decreased or ineffective respiratory effort; and/or hypoxemia ($PO_2 < 60$ mmHg or PaO_2/FIO_2 less than 200), and evidence of infiltrate on chest radiography
Impaired airway protection due to absent or reduced gag reflex, airway obstruction, recurrent aspiration
Seizures lasting longer than 5 min
Therapeutic hyperventilation
Surgical craniotomy

hemorrhage have a decreased level of consciousness and require intubation [58]. In one study, 156 of 527 patients (29.6%) with ICH required mechanical ventilation [58]. All patients with infra-tentorial and 83% of those with supratentorial ICHs were intubated for neurologic deterioration; 63% required intubation on presentation. In another study [59] of 224 patients with acute stroke admitted to neuro-ICU, 131 met the inclusion criteria for endotracheal intubation; 90 patients (69%) had spontaneous ICH. The reason for intubation was reduced level of consciousness in 84.0% of patients in the study, hypercarbia/apnea in 6.1%, hypoxia in 4.6%, bulbar dysfunction in 2.3%, hyperventilation in 1.5%, status epilepticus in 0.8%, and surgery in 0.8%. The median time from stroke to intubation was less than 1 day (range 0–13 days).

6A. Time to Intubation

The time to intubation has been used a quality parameter in several other clinical conditions requiring emergent intubation. The time interval of 30 min between documented indication and intubation was selected arbitrarily. The NRCPR's Scientific Advisory Board and the Emergency Cardiac Care Committee of the AHA have recommended that invasive airway placement should occur within 5 min, and that time to invasive airway should be considered a "Process Gold Standard" for resuscitation [60]. One study [61] examined the association between time to invasive airway placement and patient outcomes after in-hospital cardiopulmonary arrest in 25,006 patients. The mean time to invasive airway placement was 6 min and early airway placement was associated with better odds of 24-h survival but not with survival at later intervals. In a retrospective cohort study of 693 patients, faster intubation times increased the odds of survival in pre-hospital cardiac arrest [62]. The time to intubation has been used as a quality indicator in assessment of delays of providing preclinical rescue procedures among patients with TBI [63]. In an analysis of 3,804 patients with TBI [64], early mechanical ventilation was associated with higher likelihood of achieving PCO(2) range 30–49 mmHg which in turn was associated with higher survival. In one study [65], the increased use of early intubation and mechanical ventilation during transfer reduced the rate of hypoxia and hypotension with subsequent improvement in survival in TBI patients. However, the current quality indicator does not promote "rush intubation-within 5–10 min" but encourages "timely controlled intubation-within 30 min" to minimize complications such as oro-pharyngeal injury, aspiration, glottic edema, and esophageal intubation [66]. A small delay in endotracheal intubation for appropriate assessment and initial treatment did not increase adverse outcomes in patients with cardiopulmonary arrest [67].

Category 7: Treatment of Clinically Significant Intracranial Mass Effect or Transtentorial Herniation (TTH)

The threshold for treatment was either newly observed unilateral or bilateral pupillary enlargement or two spontaneous ICP elevation >20 mmHg persisting for >5 min (if ICP monitoring is available for clinically appropriate reasons such as intraventricular drainage or local standard of care), based on previous clinical trials [68, 69]. Patients with stroke were randomized to either mannitol or hypertonic saline or single arm treatment with hypertonic saline for an increase in ICP of 20 mmHg ($n = 18$), pupillary abnormality ($n = 3$), or a combination of both ($n = 1$) in 22 episodes in one trial [68] and a rise in ICP >25 mmHg in 22 episodes, a newly observed pupillary abnormality in 3 episodes, and both in the remaining 5 of the 30 episodes in the second study [69]. The syndrome of TTH represents a usually fatal consequence of supratentorial mass lesions including ICH [70–72]. While there is considerable overlap in occurrence and treatment, TTH can occur in the absence of global intracranial hypertension [73] and cause global oligemia in brainstem and supratentorial gray and white matter despite adequate CPP [74]. Therefore, TTH as a treatment indication and its reversal as an endpoint is an important strategy among patients with supratentorial mass occupying lesions [75].

7A. Success of Treatment

The success of treatment was determined by clinical reversal of TTH, defined as a reduction in pupillary diameter with return of light responsiveness associated with an increase in GCS of ≥ 2 points, or ICP value <20 mmHg within 1 h of detection if ICP monitoring is available. Schwarz et al. [68] found that treatment success defined by these parameters was achieved in all 22 episodes among patients with stroke treated with 75 ml of 10% saline administered over a period of 15 min. In a previous randomized trial [69], treatment success using the same definition was observed in 10 of 14 episodes treated with mannitol and 16 of 16 episodes treated with hypertonic saline in patients with stroke. Small clinical [73, 76, 77] studies have demonstrated that TTH can be reversed with aggressive medical and surgical management. We had previously performed a prospective study in 28 consecutive patients after reversal [73], where as soon as an episode of TTH was recognized, manual hyperventilation was initiated with a ventilation bag along with emergent intubation if the patient was not already intubated to maintain $PaCO_2$ between 25 and 30 mmHg. An osmotic agent, usually mannitol (0.5–1 g/kg), was administered at the same time intravenously. A second osmotic agent, hypertonic saline,

was administered, if adequate response is not observed with the first osmotic agent after 10 min. Herniation was reversed by using a combination of hyperventilation, mannitol, and hypertonic saline. The in-hospital mortality was 60% ($n = 15$) with brain death being the cause of death in 13 patients. Of note, seven of the 13 survivors were functionally independent after a mean follow-up period of 11 months.

7B. Time to Treatment

The need for time sensitive intervention with either reversal of TTH or reduction in ICP has been recognized in previous studies. Timing of treatment was critical in rats subjected to global cerebral ischemia treated within 1.5 min, but not at 32 min. Early treatment, after reperfusion with a bolus dose of 7.5% hypertonic saline resulted in improved long-term survival, neurologic function, and neuronal survival [78]. Andrews and Pitts [76] had found that rapid recovery of papillary responsiveness after hyperventilation and infusion of mannitol correlated with functional recovery in 153 patients with TTH secondary to TBI. Schwarz et al. [68, 69] graded success based on response within 30 min of initiating treatment based primarily on personal experiences and general recommendations. We used 1 h as the time period to define treatment success to allow ascertainment of maximum effect of mannitol or hypertonic saline. Schwarz et al. [69] had observed that the greatest decrease in the ICP from baseline level occurred after 45 min, by 24% in the patients with stroke treated with mannitol. In the second study [68], Schwarz et al. found that the maximum ICP decrease was seen 35 min after the start of infusion. Koenig et al. [79] also defined treatment success was defined by clinical reversal of TTH, defined as a reduction in pupillary diameter with return of light responsiveness associated with an increase in GCS of $\geq$2 points, occurring within 1 h of 23.4% saline administration in 68 patients who suffered 76 episodes of TTH. The TTH was reversed in 57 of the 76 treated episodes. Vialet et al. [80] defined treatment failure based on failure to reduce ICP $<$25 mmHg within a 1 h time frame (two 20 min infusions and two 10 min post-treatment response assessment) in a randomized trial comparing isovolume infusions of either 7.5% hypertonic saline solution or 20% mannitol in patients with intracranial hypertension related to TBI.

7C. Sustained Effective Treatment of Persistent Clinically Significant Intracranial Mass Effect or Intracranial Hypertension

Persistent clinically significant intracranial mass effect or intracranial hypertension is common after the first episode of intracranial hypertension or TTH and requires additional treatment including intraventricular drainage, hypertonic saline infusion, repeated mannitol boluses, and neurosurgical evaluation. We defined treatment success as absence of *brain death status* within 7 days of a newly observed unilateral or bilateral pupillary enlargement or two spontaneous ICP elevation $>$20 mmHg persisting for $>$5 min (if ICP monitoring was available). The parameter was selected to assess the intensity of care and its effectiveness after initial successful treatment. Studies have reported a high number of repeat interventions among patients with stroke who undergo treatment of intracranial hypertension or TTH episode: mean 3.3 events per patient, range 1–7 events [68] and mean 2.8 events per patient, range 1–4 [68] in two separate studies. A total of 16 patients among the 28 consecutive patients (6) had a second episode of TTH after reversal of first episode (mean interval 88.2 h, range 23–432 h). Second episode of TTH was associated with increased in-hospital mortality. All eight patients who had care withdrawn suffered brain death after a mean period of 141 h after TTH reversal. In contrast, 7 of 20 patients died among those with continued care including hypertonic saline infusion for a mean period of 30 h after first reversal. Koenig et al. [79] reported additional medical therapies instituted within 24 h of TTH in addition to 23.4% saline including hyperventilation in 70%, mannitol in 57%, continuous infusion of hypertonic saline (2% or 3% sodium chloride/acetate) in 33%, propofol in 62%, and pentobarbital in 15%. Surgical therapies undertaken in this time period included ventriculostomy catheter placement in 21 patients (28%) and decompressive hemicraniectomy in 14 patients (18%). Among the 57 patients with initially successful reversal of herniation, 26 (46%) had a second herniation event prior to death or discharge. Unsuccessful reversal of TTH and recurrent TTH during the hospitalization were predictors of in-hospital death.

7D. Routine Use of Manitol, Hypertonic Saline, and ICP Monitoring (Not Recommended as Adjunct Measure)

Routine treatment with mannitol or hypertonic saline was not recommended because two randomized trials have failed to demonstrate any benefit on regional cerebral blood flow, neurological improvement, mortality, and functional outcomes with routine repeated use of IV mannitol boluses [81, 82]. In a systematic review of patients with ischemic stroke or ICH [83], mannitol was administered intravenously in a dose of 0.8–0.9 g/kg for 10 days in 36 patients; 41 patients were in control group. Fourteen of 41 controls (34%) and 12 of 36 mannitol-treated patients (33%) improved, whereas the number of those whose condition worsened was 18 of 41 (44%) and 16 of 36 (44%). Therefore, the present data only supports the short-term use

of mannitol in patients with ICH under special circumstances such as TTH or acute neurological deterioration associated with high ICP or mass effect.

Routine use of ICP monitoring was not measured as a quality parameter because the current parameters were limited to non-surgical interventions and value of ICP monitoring remains controversial. ICP monitoring maybe helpful in identifying the risk of neurological deterioration [84] in patients with impaired level of consciousness or neurological deterioration suspected due to elevated ICP [85]. Preoperative measures of ICP were significantly related to delayed neurological deterioration, death within 3 days, and Glasgow Outcome Scale (GOS) at neurosurgical discharge [84] in 62 patients with ICH. However, no relationship was found between preoperative measures of neither ICP nor CPP and outcome at 6 months. Mechanical damage and even TTH can be seen in the absence of a global increase in ICP due to the localized mass effect. In a study of 60 patients undergoing ICP monitoring, ICP elevation was not seen in two-thirds of the patients who died [86, 87].

Category 8: Treatment of Repetitive Seizures and Status Epilepticus

Clinical seizures are reported in 8% of patients with ICH [88] within 1 month of symptom onset and frequently associated with lobar location or hematoma enlargement. However, continuous electroencephalographic (EEG) monitoring demonstrated electrographic seizures in 28% of the patients with ICH [89] during the initial 72 h after admission with four times as many subclinical seizures than clinical seizures. Seizures were associated with neurologic worsening and with an increase in midline shift, and worse outcomes. In another study of 45 patients with ICH [90], subclinical seizures and non-convulsive status epilepticus were detected in 13% and 9% of the patients, respectively. Uninterrupted convulsive and non-convulsive seizures (status epilepticus) is in the ICU patients is associated with high mortality [91]. Therefore, a low threshold for obtaining EEG studies and use of anticonvulsants in patients with ICH may be advisable.

8A. Criteria for Treatment

Continuous or repeated seizure activity for more than 5 min without recovery of consciousness was used to define the need for aggressive anticonvulsant treatment consistent with previous studies [92, 93]. Alldredge et al. [92] stated that "at a practical level, the definition of status epilepticus should not be the topic of bedside debate and seizures should be terminated as soon as possible". The Epilepsy Foundation of America working group and several major recent studies have defined status epilepticus as "any seizure lasting for 30 min or longer or intermittent seizures lasting >30 min from which the patient did not regain consciousness." In the hospital-based Veterans Administration study [94], the definition was based on two or more generalized convulsions without full recovery between seizures or continuous convulsive activity for more than 10 min. Treatment after 5 or 10 min of continuous seizure activity is currently considered essential to protect against neuronal and systemic damage from ongoing seizure activity. The definition with the shortest interval to diagnosis was used with the understanding that a higher proportion of episodes that may not be seizures and those that will spontaneous resolve will be treated. However, there is no evidence that overtreatment in this scenario is harmful. Initiating treatment with lorazepam or diazepam within 5 min of seizure onset was associated with higher rates of status epilepticus termination by the time of arrival at the ED (59%, 43%, and 21% of patients given lorazepam, diazepam, and placebo) [92].

8B. Treatment Success

Expedient cessation of seizure activity is a time sensitive endpoint for therapeutic intervention denoted by cessation of all motor seizure activity within 20 min after the initiation of treatment and if there was no return of seizure activity during the next 40 min similar to Veterans Affairs medical centers trial [94]. Status epilepticus was considered to end at the time convulsive seizures ceased if the patient subsequently regained consciousness and ongoing when seizures were clinically evident, clinical seizures ended but the patient remained comatose and an EEG indicated ongoing electrical seizure activity, or when a patient remained unconscious and subsequently had a convulsive seizure requiring treatment with an antiseizure drug. In the Veterans Affairs medical centers trial [94], patients in whom treatment success was not achieved with the study treatment had a two-fold higher rate of mortality compared with those in whom treatment success was achieved. The Working Group on Status Epilepticus defined refractory status epilepticus based on established seizure activity for over 20 min and used it to identify failure of initial therapy [95]. Another quality measure that may be investigated further is mandatory use of continuous EEG monitoring in patients with all motor activity continuing within 20 min or any return of seizure activity within 40 min. Status epilepticus becomes progressively less responsive to treatment as seizures continue. In a review of status epilepticus in San Francisco in the 1980s, seizures were stopped by first-line therapy (usually diazepam followed by phenytoin) in 80% of patients when treatment was begun within 30 min of the onset of the seizures [96]. In contrast, the response rate was less than

40% when treatment was begun 2 h or more after the onset of the seizures.

8C. Choice of IV Medications (Not Recommended as a Quality Indicator)

Aggressive treatment of seizure in the ICU is recommended to reduce the risk of secondary neurological injury [97]. The first-line drug of choice is IV lorazepam in several guidelines because some studies have suggested that lorazepam may be associated with a reduced rate of seizure recurrence [98, 99] followed by phenytoin or fosphenytoin as first-line and second-line therapies for status epilepticus [100]. Specifying a specific agent is premature because no significant differences in outcome at 30 day was seen among patients with overt status epilepticus or those with subtle status epilepticus randomized to either IV treatment with lorazepam, phenobarbital, phenytoin, or diazepam followed by phenytoin conducted at 16 Veterans Affairs medical centers and 6 affiliated university hospitals [94]. Several guidelines have considered both lorazepam and diazepam as acceptable options for initial treatment of status epilepticus [95, 101].

8D. Treatment Success by Preventing Seizure Recurrence

No recurrence of overt or subtle seizure 12-h after first seizure was another endpoint used to categorize the sustained control of seizures secondary to implementation of antiepileptic drugs similar to criteria of Veterans Affairs medical centers trial [94]. In another study [102], the latency between onset of seizures and initiation of IV levetiracetam correlated with clinical response to AED. Administration of IV levetiracetam within 12 h after the onset of seizures resulted in higher rate of seizure termination and lower rates of seizure recurrence, and death or continuing coma/stupor. Complete recovery of consciousness as a measure of absence of seizure recurrence is confounded by low rate of patients who meet the endpoint with delayed recovery in consciousness unrelated to seizure activity and potentially drug-induced impairment of consciousness [94]. Sixty-seven of the patients with overt status epilepticus (17%) regained full consciousness before the end of the 12-h study period and none of the patients with subtle status epilepticus completely regained consciousness during the 12-h study period.

8E. Prophylactic Anti-Epileptic Drugs (AED) (Not Recommended as a Quality Indicator)

The use of prophylactic AED was not considered a measure due to the controversy regarding such practice. A 30-day course of prophylactic anticonvulsants is recommended in patients with lobar ICH or those who develop seizures [9, 10] based on risk reduction suggested by observational studies [88]. In an analysis of 295 patients, AEDs were initiated on 23 patients (8%) without documented seizure during the first 10 days of the trial. In logistic regression, initiation of AEDs was robustly associated with poor outcome (after adjustment for other known predictors of outcome) after ICH.

Category 9: Rapid Reversal of Elevated International Normalized Ratio (INR)

Anticoagulant related ICH accounts for 10–12% of all ICH [103] and appears to be increasing due to increasing prevalence of atrial fibrillation and higher rates of warfarin use. An elevated INR is observed in up to 75% of the patients with anticoagulant related ICHs [104, 105]. In one study of 71 patients with anticoagulant related ICH [106], 15 patients had an INR of >4.8, and 11 had an INR >2.8; the 45 remaining patients had INR values within the therapeutic range. In another study of 42 patients [107], median INR at admission was 3.1 (range 1–12). Higher rates of expansion and 3 month mortality were associated with anticoagulant related ICH. In a multicenter study, neurological deterioration during the first 24–48 h was seen in almost half of the patients with anticoagulant related ICH and a high mortality rate of 64% by 6 months [108]. Multiple guidelines suggest that patients diagnosed with anticoagulant related life-threatening hemorrhage, including ICH, should receive emergent therapy to lower their INR [109]. In a report of 102 patients with anticoagulant related ICH [110], the INR was <2.0 in 25, 2.0–3.0 in 43, and >3.0 in 32 patients. The mortality at 3 months according to initial INR value was as follows: <2.0 40%, 2.0–3.0 49%, and >3.0 66%. Increasing intensity of anticoagulation was strongly associated with increasing risk of death.

9A. Rapid INR Reversal (Within 2 h)

INR reversal (<1.4) within 2 h of first elevated INR >1.4 was recommended as a quality parameter. Huttner et al. [111] reported upon 55 patients who were treated within 0.9 (median 1) hour after admission using a combination of vitamin K (VAK), fresh frozen plasma (FFP), and/or prothrombin complex concentrates (PCCs). Early INR reversal (<2 h) was achieved in 33 of 55 patients. A trend for reduced extent of hematoma growth among patients with early INR reversal was observed compared with those without early reversal (38% vs. 54%). An increased INR after 2 h was an independent predictor of hematoma expansion in the multivariate model. PCC was associated with a reduced incidence and extent of hematoma growth compared with FFP and vitamin K presumably related to a

more rapid INR reversal. Goldstein et al. [112] reported upon 69 patients with anticoagulant related ICH with the initial median INR of 3.0 (range 2.2–3.9) and follow-up INR of 1.5 (range 1.4–1.7) at a median time of 300 min. The timing of FFP administration was associated with successful INR reversal. Median time to first dose of FFP was significantly lower among patients who had an INR $\leq$1.4 within 24 h (90 min compared with 210 min). Every 30-min delay in FFP administration was independently associated with a 20% decrease in the probability of successful INR reversal within 24 h. Rapidity of administration of vitamin K had a similar independent effect in this model. However, early time to treatment and successful INR reversal did not improve outcomes. Rapid reversal of INR has also permits urgent surgical evacuations in neurologically deteriorating patients with anticoagulant related ICH. Early reversal and evacuation was associated with a high rate (65%) of favorable outcomes in patients with a prominent midline shift (with or without TTH) in one study [113].

9B. Multiple Agents for Reversal of INR

At least two reversal agents administered within 2 h of first INR $>$1.4 were recommended without specifying the agents based on previous recommendations [11]. A combination of IV vitamin K, PCC, or FFP and fVIIa is usually recommended without a clear evidence for superiority of one regimen over another [103]. The AHA/ASA Stroke Council [9] recommends that PCC, factor IX complex concentrate, and rFVIIa normalize the laboratory elevation of the INR very rapidly and with lower volumes of fluid than FFP but with greater potential of thromboembolism. FFP is another potential choice but is associated with greater volumes and much longer infusion times (Class IIb, LOE B). Patients with anticoagulant related ICH should be treated with IV vitamin K to reverse the effects of warfarin and with treatment to replace clotting factors (Class I, LOE B). PCC or fVIIa can achieve rapid reversal although the INR may increase in subsequent hours due to short half-lives of these agents and it requires monitoring. In one study, an early INR reversal (within 2 h) was achieved in 84%, 39%, and 0% of the patients treated with PCC, FFP, and vitamin K, respectively [111]. A retrospective study [114] compared the outcomes of neurosurgical patients with ICH treated with FFP and fVIIa and those managed with FFP. INR normalized over a mean period of 7 h and 47 h in patients treated with and without fVIIa, respectively. The INR decreased from a mean of 2.7 to 1.1 after administration of rFVIIa measured between 2.5 and 7.5 h after administration of rFVIIa in seven patients with ICH [115]. In a retrospective comparison [116], the median times from presentation to an INR of less than 1.3 were 9 and 32 h in the patients treated using vitamin K and FFP with ($n = 15$) or without rFVIIa ($n = 12$), respectively. It should be noted the use of rFVIIa within 4 h of symptom onset among ICH patients without known use of oral anticoagulants reduced hematoma expansion but did not improve survival or functional outcome [117]. The rate of severe disability or death at 3 months was 24% in the placebo group, 26% in the group receiving 20 μg/kg, and 29% in the group receiving 80 μg/kg of rFVIIa. Therefore, the current recommendation is only relevant to ICH patients with elevated INR secondary to oral anticoagulants.

Category 10: Treatment of Elevated Serum Glucose Concentration

Elevated SGC has been associated with hematoma expansion [118] and poor clinical outcomes [119] in clinical studies.

10A. Threshold for Initiating Treatment

A value of SGC of $>$200 mg/dl was chosen to provide a value with consistent adverse effect on outcome in patients with ICH and used to define conventional treatment in randomized trials of glucose control is stroke patients [120]. The targets for treatment of hyperglycemia provided in guidelines for acute stroke have varied from 185 to 300 mg/dl [9, 121] and from $>$150 to $>$250 mg/dl in studies evaluating treatment of hyperglycemia in other diseases [122]. The criteria for implementation of insulin treatment vary, with EUSI guidelines advising intervention if SGC exceeds 180 mg/dl, whereas the ASA now advocates a threshold of 200 mg/dl [123]. In an audit of acute neurological stroke care performed across 22 countries by the European Federation of Neurological Societies, the mean threshold for intervention was 190 mg/dl [123]. A study evaluated the effects of diabetes and admission hyperglycemia in among 764 patients with ICH in relation to 30-day and 3-month mortality [124]. Mean SGC was higher and lower than $\approx$200 mg/dl in noncomatose diabetic subjects who died or survived at 30 days, respectively. The Acute Brain Bleeding Analysis Study found that the highest quartile of glucose level ($>$167 mg/dl) was an independent risk factor of early mortality in 1,387 patients with ICH [119, 125]. However, studies have chosen a lower SGC treatment target ($>$150 mg/dl) with no clear evidence of improvement in prognosis [126]. A pilot study [127] compared the cerebral hemodynamics and neurochemical changes (measured by microdialysis) in ICH patients post-operatively who underwent conventional SGC control and intensive SGC control with continuous titrated insulin therapy. The mean CPP and extracellular glucose did not differ significantly between the two groups

of patients although concentrations of lactate and pyruvate were lower in the intensive treatment group. An analysis of the 933 UK Glucose Insulin in Stroke Trial [128] did not demonstrate a reduction in mortality among patients presenting within 24 h of stroke onset (admission plasma glucose concentration between 108 and 306 mg/dl) randomized to receive variable-dose-insulin (target 72–126 mg/dl) or saline for 24 h. There was no significant reduction in mortality at 90 days between the two groups although separate analysis for patients with ICH was not reported.

10B. Time to Achieve Target SGC

The time to first hourly SGC within goal range has been used as a quality measure in several studies [129]. The time needed to capture the defined target was reported in 25 out of 49 studies and was represented as mean or median [122]. The therapeutic goal of the treatment has ranged from 72 mg to 144 mg/dl [122, 130]. Although a target of 140 mg/dl was recommended but any pre-defined target was considered acceptable. Other measures used to define glycemic control such as proportion of patients with glucose in the desired range, mean SGC, and frequency of hypoglycemic episodes were considered less feasible for audits. Hypoglycemia events are very rarely symptomatic in trials conducted in patients with acute stroke [120, 131]. A reasonable time to achieve the target glucose was considered 4 h after detection of hyperglycemia. The Diabetes Mellitus Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study found that the SGC decreases relatively rapidly during the first hours after initiation of treatment, with a nadir 6 h after the start of the infusion [132]. In another study, 29 diabetic patients with acute MI, the main endpoint was to achieve therapeutic target within 4 h of treatment [133]. An analysis of the first 452 patients recruited to GIST-UK suggested that differential glucose lowering was evident at 8 h after instituting treatment in the intensive glucose lowering group although some delay was attributable to higher SGC at baseline among the intensive treated group [134].

10C. Absence of Recurrence Within 72 h

The first 72 h after onset represents a period of increased vulnerability to both primary and secondary (recurrent) hyperglycemia. Avoidance of hyperglycemia throughout the first 72 h of symptom onset was chosen as the therapeutic target. The quality indicator assesses the effectiveness of appropriate maintenance treatment for hyperglycemia. The measure is a qualitative analogue to area under the curve for SGC control over 72 h after initiation of treatment used in prospective studies. In an analysis of 60 ICH patients who were enrolled in the ATACH study, that initial mean glucose concentration was not associated with functional outcome, or hematoma expansion. However, patients with SGC decline within 72 h had a lower relative risk of symptomatic hematoma expansion and death or disability at 3 month. In another study, higher initial and 48-h maximum glucose concentrations were significantly associated with poor functional outcome at hospital discharge among 88 patients with ICH associated with high INR [135]. Aggressive treatment of SGC using IV insulin during the first 72 h after ICH was used as therapeutic goal in a prospective observational study [126]. Hyperglycemia after the first 48–72 h is also less frequent in acute stroke and may not require aggressive treatment [136]. Previous studies evaluating the value of intensive SGC control in the medical ICU in non-stroke patients have also chosen the first 72 h as the period to monitor and initiate treatment [137].

Category 11: Treatment of Hyperpyrexia

Hyperpyrexia in the first 12–24 h after stroke onset is associated with poor functional outcome. Mortality was lower and outcome better in the absence of hyperpyrexia in 390 patients with acute stroke admitted within 6 h [138]. For each degree increase in body temperature, the relative risk of poor outcome increased almost two folds [138].

11A. The Definition of Hyperpyrexia

The definition of hyperpyrexia ($T \geq 38.3$°C on two consecutive measurements 1 h apart) was based on definition used in a previous randomized trial comparing the Arctic Sun System and the Sub Zero for achieving normothermia among patients admitted to the neuro ICU [139]. Using the threshold, Arctic Sun treatment resulted in an 81% reduction in percent time febrile, a 73% reduction in time to attain normothermia, and trend towards improvement in GCS score at the completion of the trial [139]. This threshold is also considered indication for starting antipyretics and investigation for infections in routine practice [140]. The period to detect and treat hyperpyrexia as a quality measure was inclusive of the first 72 h after symptom onset because hyperpyrexia in that time period after ICH was associated with a poor outcome [140]. In the Paracetamol (Acetaminophen) In Stroke (PAIS) trial, patients with ischemic stroke or ICH were randomly assigned treatment with paracetamol (6 g daily) or placebo within 12 h from symptom onset. The results did not support routine use of high-dose paracetamol in patients with acute stroke but there was some beneficial effect on functional outcome in patients admitted with a higher body temperature 37–39°C [141].

11B. Time to Achieve Target Temperature

The time to achieve target temperature has been used in previous studies [142] and maybe more feasible for chart based audits than other measures such as the weighted sum of changes in body temperature over the evaluation period [142] and area under the curve for fever burden [139, 143, 144]. Four hours was chosen as the time to achieve target temperature based on the results of randomized trial comparing treatment with either 1,000 mg of acetaminophen or placebo, given six times daily in 102 patients with acute ischemic stroke. The lower mean body temperature in the active treatment group was different compared with placebo treatment within 4 h and was maintained throughout the next 20 h [145]. In another study, aspirin 500 and 1,000 mg and acetaminophen 500 and 1,000 mg compared with placebo in adult patients with acute febrile respiratory infection and chose change body temperature from the time of treatment (baseline) to 4 h after dosing as primary outcome [143]. All active treatments were significantly superior to placebo in terms of the primary efficacy outcome. The Neurocritical Care Fever Reduction Trial Group considered a temperature of $>38°C$ for 4 continuous hours to define persistent fever that required CoolGard/Cool Line catheter system (Alsius, Irvine, CA) [144].

11C. Absence of Recurrence Within 72 h

The first 72 h after onset represent a period of increased vulnerability to both primary and secondary (recurrent) hyperpyrexia. The quality indicator assesses the effectiveness of identification of source of fever, institution of appropriate treatment, and appropriate maintenance treatment for hyperpyrexia. The measure is a qualitative analogue to area under the curve for fever control over 72 h after initiation of treatment used in prospective studies.

Category 12: DVT Prophylaxis

The quality indicator was recommended due to the relatively high prevalence of DVT among patients with ICH which can be reduced with appropriate preventive strategies. DVT was detected a total of 21 patients (40%) among 52 patients studied with ultrasonography to detect DVT within 72 h of onset of ICH and after 2 weeks [146].

12A. Time of Initiation of DVT Prophylaxis

The first 48 h after symptom onset was considered the appropriate time to initiate prophylaxis based on consistent safety and effectiveness data provided by clinical trials in ICH patients. It remains unclear whether starting low-dose heparin after the time frame when most hematoma expansions occur (first 24 h) as in the trial by Boeer et al. [147] is appropriate or additional confirmation by serial CT scans to document stability (mentioned under Category 2) of hematoma is required. In one study of 68 patients with ICH [147] the effect of low-dose subcutaneous heparin ($3 \times 5{,}000$ U/day) treatment beginning on the second (added after completion of first two tiers), 4th or 10th day was investigated. Patients with bleeding diathesis, severe cerebral edema and deep coma, and marked hypertensive response were excluded. Early (day 2) low-dose heparin medication significantly lowered the incidence of pulmonary embolism (odd ratio 9.2). There was no overall increase in the incidence of hematoma expansion as assessed by serial CT scans. In another study, ICH patients [148] were randomized to receive elastic stockings (ES) alone or combined with intermittent pneumatic compressions (IPC) within 48 h of admission. Asymptomatic DVT detected by venous ultrasound in 11 (16%) and 3 (5%) of patients treated with ES or ES with IPC, respectively (relative risk reduction of 0.29). Studies that have initiated prophylaxis after first 48 h have a prominently reduced benefit. A study compared 232 patients who received and 175 who did not receive low-dose subcutaneous low molecular weight heparin (LMWH) treatment after first 48 h [149]. The 3-month death rate was 19 and 21%, respectively. Hematoma enlargements occurred in 9% and 7% of the treated and untreated patients, whereas symptomatic venous thromboembolic complications were observed in 3% and 2%, respectively. Another study randomized 75 primary ICH patients [150] to subcutaneous noxaparin sodium 40 mg/d or long ES after the first 48 h. Three and one asymptomatic DVT were observed in LMWH and ES treated groups, respectively. No hematoma enlargement was observed at 3, 7, and 21 days in both groups.

12B. Method of DVT Prophylaxis (Not Recommended as Adjunct Measure)

No clear differential benefit has been demonstrated between low molecular weight heparin, heparin, or IPC for preventing DVT among patients with ICH. DVT was significantly reduced with the addition of an LMWH compared with placebo, but rates of DVT were similar when comparing LMWH with heparin in a meta-analysis involving 12,391 unselected medically ill patients [151]. No significant differences in pulmonary embolism or death were found among heparin, LMWH, and placebo treated groups. Only an indirect comparison of low and high doses of heparin and LMWH using data from 16 trials involving 23,043 ischemic stroke patients suggests that low-dose LMWH has the best benefit/risk ratio for reducing both DVT and pulmonary embolism, without a clear increase in ICH [152].

Category 13: Dysphagia Screening

Documentation of dysphagia assessment within 72 h of symptom onset was recommended as a quality indicator. Dysphagia, defined as difficulty swallowing any liquid (including saliva) or solid material, was documented in 1,506 (51%) of the 2,983 patients with acute stroke and was associated with poor outcome [153]. It remains unclear whether the poor outcome in these patients is related to stroke severity, complications directly related to dysphagia, or both. In one study [154], severity of dysphagia predicted outcome and intercurrent complications after acute stroke independent of severity of neurological deficits. Early identification of dysphagia from screening can lead to earlier treatments and thereby reduce complications. A review of 10 studies concluded that there was evidence for screening benefit based on a reduction in pneumonia, length of hospital stay, personnel costs, and patient charges [155]. Dysphagia screen prior to oral intake has been considered one of three quality measures that were applicable to the care of both ischemic stroke and ICH in Get With The Guidelines–Stroke quality-improvement initiative [156]. Dysphagia screening is also one of the 10 performance measures in the Paul Coverdell National Acute Stroke Registry [157] with prominent statewide variation (39–51%) documented in a review of 6,867 total acute stroke admissions (9% with ICH) [158]. A review of 479,284 consecutive admissions at 905 hospitals suggested that ICH patients were more likely to undergo dysphagia screening compared with ischemic stroke and transient ischemic attack patients; 68% vs. 63% of admissions [25]. The 72-h time frame was chosen to remain consistent with the time frame recommended for enteral feeding below.

13A. Method of Dysphagia Screening (Not Recommended as a Quality Indicator)

Many methods have been proposed to evaluate for presence and severity of dysphagia including bedside dysphagia screening tool [159], oxygen desaturation during swallowing [160], fiberoptic endoscopy [154], and videofluoroscopic assessment of swallowing [161]. The correlation between bedside evaluations and videofluoroscopic assessment or fiberoptic endoscopy was moderate to high in a review of 26 studies [162]. Therefore the selection of test for dysphagia screening may vary between institutions depending upon expertise, protocols, and availability of invasive tests.

Category 14: Feeding (Nutrition) Initiation

The recommendation that the enteral route be used preferentially for nutritional support is based on cost information and on studies in trauma patients that demonstrate the superiority of enteral over parenteral nutrition [163]. Souba [163] recommended that enteral feeding (target of 22 to 30 kcal per kilogram of body weight per 24 h) with balanced composition be started as early as possible when patient was hemodynamically stable. Poor nutrition has been documented to adversely affect functional outcomes after strokes [164]. A recent Cochrane Report concluded that protein and energy supplementation produces small but consistent weight gain and decreased mortality in stroke patients [165].

14A. Time to Initiate Enteral Feeding

The first 72 h after symptom onset was considered the appropriate time to initiate enteral feeding based on consistent safety and effectiveness data provided by clinical trials in stroke patients. In one study, length of stay was shorter the among patients receiving enteral nutrition within 72 h of admission, compared with those fed later than 72 h after admission [166]. A large International study [167] randomized 859 patients into either enteral tube feeding (via the clinician's preferred tube) as soon as possible or to avoid any enteral tube feeding for at least 7 days. Of the 429 patients allocated to early tube feeding, 369 (86%) received tube feeding within 3 days. Early tube feeding was associated with an absolute reduction in risk of death of 6% and a reduction in death or poor outcome. Another concurrent trial [167] randomized 321 patients with dysphagia to either feeding via percutaneous enteral gastrostomy (PEG) or nasogastric tube within 3 days of enrollment. PEG feeding was associated with an absolute increase in risk of death of 1% and an almost 8 fold increased risk of death or poor outcome. The investigators concluded that dysphagic stroke patients should be offered enteral tube feeding via a nasogastric tube within the first few days of admission. Also, for enteral feeding within the first 2 or 3 weeks, nasogastric feeding should be the chosen route unless there is a strong practical reason to choose PEG feeding [167].

Category 15: Gastric Ulcer Prophylaxis

The quality indicator was recommended due to the relatively high prevalence of gastric ulcers among patients with ICH which can be reduced with appropriate preventive strategies. The value of gastric ulcer prophylaxis in critically ill patients has been demonstrated in several trials [168]. A review of 63 relevant randomized trials demonstrated that prophylaxis with histamine2-receptor antagonists reduced overt gastrointestinal bleeding and clinically important gastrointestinal bleeding among critically ill patients [169]. Sucralfate may be as effective in reducing bleeding as

gastric pH-altering drugs and may be associated with lower rates of pneumonia and mortality. Appropriate stress ulcer prophylaxis among ICU patients reduces both hospital stays and increased costs due to clinically significant bleeding [170].

15A. Time to Initiate Gastric Ulcer Prophylaxis

The first 48 h after symptom onset was considered the appropriate time to initiate prophylaxis based on safety and effectiveness data provided by clinical trials in ICH patients with an augmented benefit with early initiation. In one study, patients with ICH within 7 days of symptom onset were randomized into three groups [171]: (1) ranitidine group receiving ranitidine 50 mg eight hourly i.v.; (2) sucralfate group receiving 1 g six hourly p.o.; and (3) placebo group receiving placebo solution. Gastric hemorrhage occurred in 11 (23%), 5 (11%), and 7 (14%) of patients in placebo, ranitidine, and sucralfate treated groups, respectively. Occurrence of gastric hemorrhage was significantly related to death. Death occurred in 13 (28%), 5 (11%), and 12 (25%) of patients in placebo, ranitidine, and sucralfate groups, respectively, with direct relationship to gastric hemorrhages. The incidence of gastric hemorrhages increased with the delay in starting treatment. The frequency of gastric hemorrhage was 3% in the group admitted within 48 h, 9% in 3–5 days and 21% in those patients admitted after 5 days. Pneumonia occurred in ranitidine group in 2 (4%), sucralfate in 5 (10%) and placebo in 5 (11%) patients and there was no significant group difference.

The value of early initiation of gastric ulcer prophylaxis was also demonstrated in a trial [172] using serial endoscopy. The trial randomized patients to receive either sucralfate (2 g) or sterile water every 8 h via the nasogastric tube. At the time of ICU admission, the frequency of gastric ulcers (as assessed with the endoscope) was 22%. No ulcers were detected at admission. By day 3, the frequency had increased to 38% in sucralfate and 89% in sterile water group.

It should be noted that none of the patients with ICH in the trial by Misra et al. [171] required mechanical ventilation. Pharmacologically increasing gastric pH may increase the risk for developing pneumonia in mechanically ventilated patients in the ICU [173]. Because mechanically ventilated patients are also at high risk for stress ulcers [174], gastric pH based titration may be required in such patients [175]. One study [176] noted that 60% of patients in the ICU started on stress ulcer prophylaxis were continued on it upon transfer from the ICU and 31% were discharged home on prophylaxis without a new indication. Therefore, timely discontinuation may have to be considered as a quality parameter in future to reduce unnecessary drug reactions and costs.

15B. Method of Gastric Ulcer Prophylaxis (Not Recommended as Adjunct Measure)

No clear differential benefit has been demonstrated between H2 blockers, proton blockers, and sucralfate in studies recruiting patients with ICH mentioned above. Therefore, no specific method was recommended. In the review of 63 randomized trials, prophylaxis with either histamine2-receptor antagonists or sucralfate was associated with reduced overt gastrointestinal bleeding [169]. There may be differential rate of pneumonias seen inconsistently between studies. Multiple agents may be needed in patients with persistent nasogastric pH <4 and/or evidence of occult or clinical bleeding despite single agent treatment [175].

Category 16: Treatment of Persistently Elevated BP

We also used documentation of oral antihypertensive medication consideration in patients with persistently elevated BP (SBP $\geq$160 mmHg) within 7 days of arrival as a quality parameter due to benefit demonstrated in clinical trials. In the California Acute Stroke Prototype Registry [177], great variability in practices between hospitals and considerable room for improvement was noted among two-thirds of patients with acute ischemic cerebrovascular events discharged from the hospital on 1 or more antihypertensive medications. A meta-analysis of nine trials [178], demonstrated significant reduction in the rate of recurrent stroke with antihypertensive drugs in patients with stroke or transient ischemic attack. The Perindopril Protection Against Recurrent Stroke Study (PROGRESS) [179, 180] demonstrated a 28% reduction in relative risk of a recurrent stroke assigned to the angiotensin converting enzyme inhibitor (with the addition of the diuretic at the discretion of treating physicians) compared with placebo over an average of 4 years of follow-up. Treatment effects were similar in people with hypertension and those with normal BP. The ASA [181] recommends antihypertensive treatment for prevention of recurrent stroke and other vascular events in persons who have had an ischemic stroke or transient ischemic attack and are beyond the hyperacute period. The choice of specific drugs and targets should be individualized, although available data support the use of diuretics and the combination of diuretics and an ACE inhibitor.

16A. Timing of Initiating Oral Antihypertensive Treatment

An important issue is the timing of initiation or aggressive titration of oral antihypertensive treatment in patients with ICH that have chronic hypertension or undetected hypertension. Theoretically, oral hypertensives medication can be initiated at 24–48 h after symptom onset [21] because

most of the acute processes, such as ischemic vulnerability and hematoma expansion, are uncommon after the first 24 h. In the ACCESS trial [182], treatment was started with daily candesartan or placebo on day 1. On day 2, the dosage was increased two- or four-fold if BP was >160/100 mmHg. If patients in the candesartan group showed a hypertensive profile on day 7 (mean daytime BP >135/85 mmHg), candesartan was increased or an additional antihypertensive drug was added. The results support early initiation of antihypertensive treatment with gradual titration to more aggressive BP treatment targets. The JNC-7 report [183] recommends that BP be maintained at intermediate levels (around 160/100 mmHg) until neurological stability is achieved. Special circumstances such as elevated ICP, progressive cerebral edema, on-going cerebral ischemia due to occlusive vessel disease or symptomatic cerebral vasospasm, and post-operative cerebral changes require individualized management. After the first week, or when neurological stability is achieved, a more aggressive treatment can be initiated for secondary prevention of recurrent stroke [184].

16B. Choice of oral Antihypertensive Treatment and Achieving Target BP (Not Recommended as Adjunct Measure)

Both the issues are predominantly addressed in the outpatients setting and therefore were beyond the scope of the current metrics.

Category 17: Tracheostomy for Persistent Intubation, or Poor Airway Protection

17A. Timing of Tracheostomy

Early tracheostomy (within 7 days of arrival) has been emphasized recently due to availability of percutaneous tracheostomy that can be performed at bedside [185, 186]. A review of patients with infratentorial lesions including ICH concluded that an aggressive policy toward tracheostomy is justified based on the low frequency of successful extubations and high frequency of tracheostomies. The decision regarding tracheostomy should be performed by day 8 of mechanical ventilation because of the low probability of subsequent extubation or in-hospital death. In one study, the probability of successful extubation or death before extubation or tracheostomy was 67% on the day of intubation, which decreased to 6% after intubation for >8 days [187]. Another study classified severe TBI patients according to the timing of tracheostomy, subjects as early group (≤7 days; $n = 27$) or late group (>7 days; $n = 28$). Patients in the early group had a significantly shorter stay in the ICU than patients in the late group (19 vs. 26 days) and favorable trend in mortality (4% vs. 15%) despite similar characteristics [188]. In another study, 157 patients were randomized to early tracheostomy (3–5 days, $n = 127$) and 28 to late tracheostomy (10–14 days, $n = 28$). There were no significant differences between the groups; however, there were trends to more vocal cord ulceration and subglottic inflammation in the continued intubation group [189]. A systematic review evaluated all the 12 prospective studies with 406 patients that used random allocation to early tracheostomy (performed up to 7 days after admission to the ICU) or late tracheostomy at any time thereafter [190]. The timing of tracheostomy did not alter mortality significantly but led to a reduced duration of ventilation and shorter stays in ICU.

Category 18. Treatment of Hospital Acquired or Ventilator Associated Pneumonia (VAP)

Hospital acquired or VAP are a frequent cause of nosocomial infection that prolongs ICU length of stay and may increase the risk of death in critically ill patients [191, 192]. The attributable risk of VAP appears to vary with patient population and infecting organism [193]. In one study involving 144 consecutive patients with ICH [194], 41 patients (28%) developed pulmonary complications. The most common events were pneumonia (19%) and pulmonary edema (8%). Pulmonary complications lengthened the duration of hospital stay among survivors. The cost of hospitalization was also higher among those patients with ICH who developed pneumonia [195].

18A. Definition

Hospital acquired or VAP during ICU stay was defined by new or progressive radiographic infiltrate and at least two clinical features (fever, leukocytosis, or purulent tracheal secretions) based on definitions used in previous studies [196]. Studies indicate that the diagnostic criteria of a radiographic infiltrate and at least one clinical feature (fever, leukocytosis, or purulent tracheal secretions) have high sensitivity but low specificity (especially for VAP) [191, 192]. Positive quantitative cultures of distal pulmonary secretion samples, obtained by fiberoptic bronchoscopy, of bronchoalveolar lavage fluid or with a protected specimen brush or catheter (significant threshold ≥103 colony-forming units/ml) although used in several studies but was considered impractical for data acquired through chart review [197].

18B. Delay in Initiation of IV Antibiotics

Institution of IV antibiotics within 24 h of first persistent fever when meeting other criteria for hospital acquired or

VAP was selected as a quality indicator similar to previous clinical trials because delay is associated with increased mortality [197]. Iregui et al. [198] also documented an adverse outcome with initially delayed appropriate antimicrobial therapy in 107 patients with VAP. Thirty-three (31%) patients received IV antibiotic treatment that was delayed >24 h after meeting diagnostic criteria for VAP, often because of a delay in physician recognition. Patients receiving delayed IV antibiotic treatment had greater hospital mortality compared with patients without the delay (70% versus 29%). Another study of 25 patients [199], observed that mortality increased if adequate antibiotic treatment was started after the first 24 h after diagnosis. After adjusting for the number of organ failures, the length of time without adequate antibiotic treatment remained associated with mortality.

18C. Appropriate Initial Empiric Therapy

No new antibiotic substituted or added within 10 days of initiating first antibiotic was used as an indicator of appropriate selection of antibiotics due to its prognostic importance. Selection of initial antibiotic therapy is based on risk factors for specific pathogens, modified by knowledge of local patterns of antibiotic resistance and organism prevalence [191, 192, 200]. Inappropriate initial antibiotic of VAP during the first 48 h increased ICU length of stay and tended to increase crude hospital mortality when compared to appropriate initial antibiotics in a population of 111 ICU patients [201]. Another study found that mortality was higher in 44% of patients who required modification of empiric antibiotic treatment for pneumonia.

Data Collection and Analysis

An important determinant of the validity of any classification scheme is reproducibility of results by different observers. The quality indicators were displayed in a case report form that provided the variable, definition of the variable, quality parameter (such as time interval between time of ED arrival and time of first note by ED physician or designee based on documentation of contact) and a score of 1 point if the quality parameter met the threshold of appropriate performance (e.g. performed within 10 min of ED arrival) or not applicable. Other categories were listed as inadequate performance or lack of adequate documentation was denoted with 0 points. The electronic medical records of two randomly selected patients with ICH who were admitted within 24 h of symptom onset were jointly reviewed by two stroke researchers with experience in data abstraction to ensure familiarity with the data collection tool. The electronic medical records of 25 consecutive patients (exclusive of the first two patients) with ICH who were admitted within 24 h of symptom onset were independently reviewed by the same two stroke researchers. Patients who were transferred from another facility or those who underwent surgical evacuation during hospitalization were not included. The patients were identified for a previous study using International Classification of Diseases, 9th Revision, Clinical Modification codes for ICH (ICD-9-CM codes 431 and 432.9). Patients in whom ICH was known or suspected to be secondary to infection, brain tumor, vasculitis, trauma, arteriovenous malformation, rupture of berry aneurysm, or hemorrhagic transformation of prior cerebral infarction were excluded. The medical records at the study site were all electronically recorded and available for review. These included nursing vital sheet, physician orders, physician notes, nursing notes, medication, laboratory test reports, and radiological investigation reports. Interobserver reliability was determined, and the [kappa] value for agreement was calculated using Stata statistical software (Intercooled, version 6, College Town, TX). The [kappa] statistic measures agreement beyond chance among observers about a particular measure or outcome [202]. Values of [kappa] >0.80 indicate excellent agreement; 0.60–0.79 indicate good agreement (low error); 0.40–0.59 indicate moderate agreement; and values of ≤0.40 are considered poor agreement. If kappa could not be calculated due to zero cells, the proportion of agreement between positive responses was estimated.

Results

A total of 1300 (26 indicator per patientX25 patientsX2 raters) quality indicators were assessed and scored. The minimum proportion of patients meeting quality parameter ranged from 44% to 100% depending upon the variable (Table 3). The lowest performance score were observed in the early intubation and mechanical ventilation, treatment of significant intracranial mass effect or TTH, and timely acquisition of CT scan of head. The highest performance score were seen in treatment of any seizure within 2 weeks of admission, status epilepticus, and prevention of gastric ulcer. The interobserver agreement for performance pertaining to quality indicator ranged from [kappa] <0.1–1 (see Table 3). The highest agreement was on the quality indicators pertaining to status epilepticus, subtle generalized convulsive status epilepticus, elevated INR >1.4 at admission, elevated SGC (≥200 mg/dl) within 72 h, hyperpyrexia $T \geq 38.3°$ within 72 h, DVT prophylaxis, and gastric ulcer prevention, and the lowest agreement was on the quality indicator pertaining to early intubation and mechanical ventilation, or treatment of significant intracranial mass effect or TTH.

Table 3 Description, performance, and inter-observer reliability of intracerebral hemorrhage specific intensity of care quality metrics

Variable	Quality parameter	1 points if YES or not applicable	Minimum proportion of patients meeting quality parameter[a]	Agreement between raters
ED evaluation	Time interval between time of ED arrival AND time of first note by ED physician or designee or documentation of contact	Performed within 10 min of ED arrival	80%	80%[b]
Expedient acquisition of neuroimaging	Time interval between time of ED arrival AND time of CT scan acquisition	Acquired within 25 min of ED arrival OR not applicable	44%	$K = 0.20$
ICU monitoring	Time interval between time of ED arrival AND time of ICU monitoring initiation	Initiated within 10 min of ED arrival	84%	84%[b]
Avoidance of withdrawal of care/ DNR	Time interval between time of ED arrival AND DNR or withdrawal of care status	No DNR/withdrawal of care status within 24 days of ED arrival	84%	84%[b]
Avoidance of withdrawal of care/ DNR	Time interval between time of ED arrival AND DNR OR withdrawal of care status AND reasons of withdrawal documented.	No DNR/ withdrawal of care status between 24 days and 7 days of ED arrival OR status changed with reasons documented	68%	68%[b]
Treatment of acute hypertensive response	Time interval between two consecutive SBP $\geq$180 mmHg AND first SBP $<$180 mmHg recording	Achieved target range with 2. 5 h of second of the two consecutive measurements OR not applicable	92%	92%[b]
Early intubation and mechanical ventilation	Time interval between time of documentation of any of the criteria (Table 2) AND time of intubation	Initiated within 30 min of detection OR not applicable	44%	$K = 0.31$
Treatment of clinically significant intracranial mass effect or transtentorial herniation	Time interval between a newly observed transtentorial herniation or two spontaneous ICP elevation $>$20 mmHg persisting for $>$5 min (if ICP monitoring available) AND time of clinical reversal of herniation (reduction in pupillary diameter with return of light responsiveness associated with an increase in GCS score of $\geq$2 points) OR first ICP value $<$20 mmHg	Clinical reversal of hrniation, occurring within OR ICP value $<$20 mmHg within 60 min of detection OR not applicable	44%	$K < 0.1$
Treatment of clinically significant intracranial mass effect or transtentorial herniation	Time interval between herniation OR ICP elevation (see above) AND first brain death examination	No breath death status within 7 days of herniation OR ICP elevation OR not applicable	64%	$K < 0.1$
Treatment of repetitive seizures and status epilepticus (CLINICAL)	Time interval between first recorded seizure AND the time convulsive seizures ceased with improvement in level of consciousness	All motor seizure activity ceased within 20 min after the first recorded seizure and there was no return of seizure activity during the next 40 min OR not applicable	100%	$K = 1.0$
Treatment of repetitive seizures and status epilepticus (SUBCLINICAL)	Time interval between first recorded EEG ictal discharge AND EEG seizure activity ceased	All motor and electroencephalographic seizure activity ceased within 20 min after the first recorded seizure and there was no return of seizure activity during the next 40 min OR not applicable	100%	$K = 1.0$
Treatment of repetitive seizures and status epilepticus	Time interval between first recorded motor or EEG ictal discharge AND absence of recurrent overt or subtle seizure	No recurrence of overt or subtle seizure 12-h after first seizure OR not applicable	96%	96%↑
Rapid reversal of elevated INR	Time interval between first elevated internationalized ratio $>$1.4 AND first INR $<$1.4 measurement	INR reversal (INR $<$1.4) within 2 h of first elevated internationalized ratio $>$1.4 OR not applicable	92%	$K = 0.65$

Table 3 continued

Variable	Quality parameter	1 points if YES or not applicable	Minimum proportion of patients meeting quality parameter[a]	Agreement between raters
Rapid reversal of elevated INR	Time interval between first elevated internationalized ratio >1.4 AND at least two reversal agents administered	At least two reversal agents administered within 2 h of first elevated INR >1.4 OR not applicable	92%	$K = 0.46$
Treatment of elevated serum glucose concentration	Time interval between first elevated serum glucose ≥200 mg/dl AND first serum glucose in target level OR <140 mg/dl if not specified	Target glucose achieved within 4 h of high glucose detection OR not applicable	72%	$K = 0.41$
Treatment of elevated serum glucose concentration	Recurrent elevation of serum glucose (serum glucose ≥200 mg/dl) for 1 h	No recurrent hyperglycemia within 72 h of admission	72%	$K = 0.27$
Treatment of hyperpyrexia	Time interval between 1 h elevated temperature AND first temperature ≤37.2°C	Time to normothermia (first temperature ≤37.2°C) <4 h OR not applicable	80%	$K < 0.1$
Treatment of hyperpyrexia	Recurrent hyperpyrexia T ≥38.3°C on two consecutive measurements 1 h apart	No recurrent hyperpyrexia within 72 h of admission	84%	$K = 1.0$
DVT prophylaxis	Time interval between ED arrival AND institution of IPC or low dose heparin or low molecular weight heparin	Initiated within 48 h of arrival OR not applicable	52%	$K = 0.36$
Dysphagia screening	Time interval between ED arrival AND documentation of bedside or formal dysphagia assessment	Initiated within 72 h of arrival OR not applicable	60%	$K = 0.64$
Feeding (nutrition) initiation	Time interval between ED arrival AND institution of oral OR nasogastric feeding	Initiated within 72 h of arrival OR not applicable	80%	$K < 0.1$
Gastric ulcer prophylaxis	Time interval between ED arrival AND institution of prophylaxis	Initiated in selected patients within 48 h OR not applicable	96%	$K < 0.1$
Treatment of persistently elevated BP	Time interval between ED arrival AND institution of oral antihypertensive medication	Initiated within 7 days of arrival OR not applicable OR contraindication documented	88%	$K = 0.34$
Tracheostomy for persistent intubation, or poor airway protection	Time interval between first endotracheal intubation AND institution of tracheostomy	Initiated within 7 days of arrival OR not applicable OR contraindication	72%	$K = 0.51$
Treatment of hospital acquired or ventilator associated pneumonia	Time interval between first persistent fever (≥38.3°C on two consecutive measurements 1 h apart) AND institution of IV antibiotics	Institution of IV antibiotics within 24 h of first persistent fever (≥38.3°C on two consecutive measurements 1 h apart) documentation	80%	80%↑
Treatment of hospital acquired or ventilator associated pneumonia	Time interval between institution of IV antibiotics AND new IV antibiotic	No new antibiotic substituted or added within 10 days of initiating first antibiotic	68%	$K = 0.4$

Abbreviations used: *ED* emergency department, *DNR* do-not-resuscitate, *ICU* intensive care unit, *EEG* electroencephalogram, *ICP* intracranial pressure, *SBP* systolic blood pressure, *CT* computed tomographic, *GCS* Glasgow Coma Scale, *INR* international normalized ratio

[a] The score of the rater with the lowest score was used

[b] Kappa could not be calculated due to zero cells

Discussion

A method to assess and objectively grade the intensity of medical care in patients with ICH was developed and feasibility of use evaluated in the present report. The 27 quality indicators that were identified assessed performance in 18 aspects of medical care in patients with ICH. A new method must have prognostic relevance to the disease process to assist in the clinical decision-making process. The current report did not address the prognostic value of the performance measures. Some of the quality indicators were identified based on studies conducted in other disease

processes. These indicators were included because the variables of interest such as hyperglycemia, hyperpyrexia, and pneumonias have high prevalence in patients with ICH and there is evidence that these variables are associated with clinical outcome. Several indicators overlap in performance activities and may not provide additional information. Another unique aspect of the method was the use of electronic medical records (EMRs) which have the potential to become the preferred source of extraction of data for quality assurance and improvement of health-care performance [203] EMR as a source of data pertinent to quality assurance (QA) and improvement is emphasized by the recent initiatives by the National Quality Forum and health care administrations [202]. A PricewaterhouseCoopers report, titled *Transforming Healthcare through Secondary Use of Health Data*, showed that of those hospitals utilizing EMR data 59% have seen quality improvements, 42% have achieved cost savings, 36% have seen patient/member satisfaction improve, and 29% have increased revenue [202].

There are some quality measures that are already used in Get With The Guidelines–Stroke (GWTG–Stroke) quality-improvement initiative [156] and in the Paul Coverdell National Acute Stroke Registry [157]. These quality measures are predominantly reflective of care required for patients with ischemic stroke. However, the intensity of medical care is more rigorous among patients with ICH with a prominent component based on ICU care. Therefore, restricting assessment to quality measures used for ischemic stroke may limit the ability to provide a comprehensive evaluation. The Therapeutic Intensity Level (TIL) scoring system has been used to record therapeutic interventions hourly while the ICP is being monitored in patients with TBI. These interventions include sedation/paralysis, ventricular drainage, mannitol/diuretics, hyperventilation, barbiturate-induced, coma and pressors [204]. The scoring system has been used in randomized clinical trials to identify any differences in intensity of care between standard and new interventions in TBI [205]. The Therapeutic Intervention Scoring System (TISS) [206] quantifies the number of ICU interventions received by subjects based on basic activities, cardiovascular support, specific interventions, ventilator support, renal support, neurologic support, and metabolic support in the ICU. However, measurement of ICP is the only variable assessed for neurological support and may not be adequate for neurological diseases such as ICH.

The next step in development of an ICH specific intensity of care quality metrics is validation and refinement of the quality indicators and thresholds presented in the current report. Future activities may include selection and validation based on consensus of experts and/or application of the system to a large series of patients with ICH and assessment of relationship of components in isolation and as a group to outcome after severity adjustment.

Acknowledgment I thank Nauman Tariq, M.D., and Musthaq H. Qureshi, M.D., for assistance with this study, and Gabriela Vazquez PhD for her assistance in the statistical analysis. Dr. Qureshi has received funding from National Institutes of Health RO-1-NS44976-01A2 (medication provided by ESP Pharma), U-01-NS062091 medication provided by ESP Pharma), American Heart Association Established Investigator Award 0840053N, and Minnesota Medical Foundation, Minneapolis, MN.

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