Leitfaden	**Anwendung von Andexanet alfa (Ondexxya®) bei Faktor Xa-Inhibitor assoziierter intrazerebraler Blutung**
Version 1.1	Datum: 14.01.2025
Aktualisierung	Mindestens jährliche Überprüfung oder Aktualisierung bei Verfügbarkeit neuer Erkenntnisse

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Hintergrund	Andexanet alfa ist indiziert für erwachsene Patienten, die mit einem direkten Faktor-Xa (FXa)-Inhibitor (Apixaban oder Rivaroxaban) behandelt werden, wenn eine Aufhebung der Antikoagulation aufgrund lebensbedrohlicher oder unkontrollierter Blutungen erforderlich ist

Geltungsbereich	**Erwachsene** Patientinnen und Patienten mit **spontaner** (nicht-traumatischer) **intrazerebraler Blutung in Assoziation mit** der **Einnahme** der direkten Faktor Xa-Inhibitoren **Apixaban** oder **Rivaroxaban**, die an der **Universitätsklinik für Neurologie** (vordergründig betroffene Funktionsbereiche: ZZNA, NEIV, NEAB sowie NEOB) **am A.ö. LKH-Universitätskliniken Innsbruck** behandelt werden

Anwendungskriterien	Voraussetzungen • Alter $\geq$ 18 Jahre • ICH durch Neuroimaging (CT oder MRT) bestätigt • Letzte Dosis von Apixaban oder Rivaroxaban innerhalb von 18 h eingenommen
Hohe Priorität	Hauptkriterium • Neuroimaging-Biomarker, die mit einer raschen Hämatomprogression assoziiert sind – **uHG[1] $\geq$ 10 ml/h** – Spot-Sign im Post-KM CT oder etablierte Progressionsparameter in der Nicht-Kontrast-verstärkten CT (NCCT)[2] Unterstützende Kriterien • Auf Apixaban bzw. Rivaroxaban kalibrierte Anti-FXa-Aktivität $>$ 100 ng/ml oder Apixaban bzw. Rivaroxaban-Spiegel $>$ 100 ng/ml[3] • max-ICH Score $\leq$ 5[4] • Baseline-Hämatomvolumen $<$ 60 ml

[1] uHG (ml/h) Kalkulation: Volumen (cm^3 = ml) des ICH im Baseline-Neuroimaging (sABC/2 Formel) dividert durch die Zeitspanne (h) zwischen Symptom-Onset und des Baseline-Neuroimaging
[2] Lancet Neurol. 2023 Feb;22(2):159-171. doi: 10.1016/S1474-4422(22)00338-6
[3] Eine Laborbestimmung des Apixaban- bzw. Rivaroxaban-Spiegels wird vom ZIMCL als Notfallbestimmung mit einer "Turnaround-Time" von ca. 30–45 min angeboten. Die Spiegelbestimmung wird empfohlen, da das Abwarten der TAT mit der von der AHA/ASA vorgegebenen Benchmark-Zeit für die Reversierung einer Antikoagulation bei AAICH kompatibel ist.
[4] Neurology. 2017 Aug 1;89(5):423-431. doi: 10.1212/WNL.0000000000004174

Niedrige Priorität	Anwendung erfordert sorgfältige, individuelle Nutzen-Risiko-Abwägung • max-ICH Score > 5 • GCS ≤ 6 • Baseline-Hämatomvolumen > 60 ml
Kriterien, die gegen eine Behandlung mit Andexanet alfa sprechen	• Auf Apixaban bzw. Rivaroxaban kalibrierte Anti-FXa-Aktivität < 70 ng/ml oder Apixaban bzw. Rivaroxaban-Spiegel < 70 ng/ml • Geplante (neurochirurgische) Operation innerhalb der nächsten 12 h, (*ausgenommen "wenig invasive" Eingriffe wie z.B. EVD-Anlage oder Anlage von Neuromonitoring-Sonden über ein Bohrloch*) • Situationen, in denen eine CTC bzw. WLST als geeignete Therapiestrategie angesehen werden • **(Vor-) Behandlung mit gerinnungsaktiven Substanzen,** insbesondere mit **PCC**, **aPCC/FEIBA** innerhalb der letzten 7 Tage oder mit **rekombinantem aktiviertem Faktor VII (Eptacog alfa)** innerhalb der letzten 12 h • **Notwendige Applikation von Heparin in den nächsten 24 h** – Andexanet alfa führt zu einem temporären Nicht-Ansprechen auf die gerinnungshemmende Wirkung von unfraktioniertem Heparin oder niedermolekularen Heparinen (sog. "***Heparin-Resistenz***") – Dies ist insbesondere in Situationen relevant, in denen invasive Eingriffe/Operationen, welche die Applikation von (unfraktioniertem) Heparin erfordern, durchgeführt werden müssen (vgl. interventionell-radiologische Diagnostik und Therapie) – *Cave:* **Heparin-Resistenz** nach Verabreichung von Andexanet alfa ist ein **signifikanter Risikofaktor für akute, schwerwiegende thromboembolische Komplikationen** – Eine Therapiealternative zu Heparin stellen in dieser Situation direkte Thrombininhibitoren (z.B. Argatroban), welche ihren Antikoagulationseffekt unabhängig von Antithrombin III entfalten, dar • Überempfindlichkeit gegen Andexanet alfa oder Hamsterproteine
Anmerkung	In Situationen, in denen die Kriterien gegen die Behandlung mit Andexanet alfa sprechen, kann die **Applikation von 4F-PCC** in Erwägung gezogen werden • Empfohlene Dosierung 50 Einheiten/kg Körpergewicht; eine Gesamtdosis > 3000 Einheiten bedarf aufgrund des hohen thrombotischen Potentials einer sorgfältigen Nutzen-Risiko-Abwägung

Sonderfälle	Spontane intrazerebrale Blutung, assoziiert mit der Einnahme von Edoxaban • Obwohl derzeit gemäß Produktinformation keine Indikation für Andexanet alfa zur Aufhebung einer Antikoagulation durch Edoxaban besteht, kann in begründeten Fällen, insbesondere bei Erfüllung der Anwendungskriterien mit hoher Priorität, eine Behandlung im Sinne eines Heilversuchs/"Named Patient Use"[5] in Erwägung gezogen werden • Eine Leitlinien-konforme Therapiealternative stellt die Gabe von 4F-PCC in der oben angeführten Dosis dar

[5] https://www.basg.gv.at/fileadmin/redakteure/01_Formulare_Listen/I/L_I235_Information_zum_Heilversuch_Named_Patient_Use_in_Oesterreich_de.pdf

Sonderfälle (cont.)	<u>Traumatische intra*kranielle* Blutungen</u> unter Einnahme von direkten Faktor Xa-Inhibitoren • Begrenzte Evidenzlage für die Anwendung von Andexanet alfa im Vergleich zu spontanen intrazerebralen Blutungen • Da für traumatische intrakranielle Blutungen die Hämatomexpansion ebenfalls prognoserelevant ist, kann auch in diesen Situationen eine Behandlung im Sinne eines Heilversuchs/"Named Patient Use"[6] in Erwägung gezogen werden • Eine Leitlinien-konforme Therapiealternative stellt die Gabe von 4F-PCC in der oben angeführten Dosis dar

Dokumentation mit Relevanz für die Anwendungsüberlegung (vgl. auch Abschnitt Überwachung und Beurteilung)	• Zeitpunkt des Symptombeginns • Relevante Neuro-Scores: GCS, NIHSS, max-ICH Score • Neuroimaging-Ergebnis: ICH Lokalisation, ICH Volumen (sABC/2), Bildgebungs-Biomarker für Hämatomprogression (Spot Sign etc.), **Kalkulation uHG (ml/h)** • Zeitpunkt der letzten FXa-Inhibitor-Dosis (falls erhebbar) • Baseline Anti-FXa-Aktivitätsspiegel (falls verfügbar) • Details der Andexanet alfa-Verabreichung (Dosis, Zeitpunkt, eventuelle unerwünschte Ereignisse)

Dosierungsschema	Das empfohlene Dosierungsschema von Ondexxya® richtet sich nach der Höhe der von der Patientin/ dem Patienten eingenommenen Apixaban- oder Rivaroxaban-Dosis sowie nach der von der letzten Einnahme vergangen Zeit

FXa-Inhibitor	Letzte Dosis*	Zeitpunkt der letzten Einnahme*	
		< 8 h	≥ 8 h
Apixaban	≤ 5 mg	**Niedrige** Dosis	**Niedrige** Dosis
	> 5 mg	**Hohe** Dosis	
Rivaroxaban	≤ 10 mg	**Niedrige** Dosis	**Niedrige** Dosis
	> 10 mg	**Hohe** Dosis	

*Wenn die **Höhe** der letzten Dosis des FXa-Inhibitors **oder** der **Zeitraum** zwischen der letzten Dosis und der Blutung **unbekannt**m sind, gibt es laut Fachinformation **keine Dosierungsempfehlung**

Niedrige Dosis	• **400 mg Kurzinfusion** mit 30 mg/min für **15 min**, gefolgt von einer **kontinuierlichen Infusion von 480 mg** mit 4 mg/min für **120 min** – **Insgesamt 5** Ondexxya® 200 mg Durchstechflaschen
Hohe Dosis	• **800 mg Kurzinfusion** mit 30 mg/min für **30 min**, gefolgt von einer **kontinuierlichen Infusion von 960 mg** mit 8 mg/min für **120 min** – **Insgesamt 9** Ondexxya® 200 mg Durchstechflaschen
Ondexxya® Depots	• **NEIV** | Neurologische Intensivstation (Kost. St. 16305) | **Tel: 23917** – **1x 5** Durchstechflaschen zu je 200 mg Andexanet alfa
	• ANWA | Allg. und Chirurgische Intensivstation (Kost. St. 17102) | Tel: 22440 – **3x 4** Durchstechflaschen zu je 200 mg Andexanet alfa

[6] https://www.basg.gv.at/fileadmin/redakteure/01_Formulare_Listen/I/L_I235_Information_zum_Heilversuch_Named_Patient_Use_in_Oesterreich_de.pdf

Handhabung und Verabreichung	• Andexanet alfa **Durchstechflasche mit 200 mg Pulver mit 20 ml sterilem Wasser für Injektionen** rekonstituieren • Für die **Kurzinfusion 40 ml** der rekonstituierten Lösung (entspricht 400 mg Andexanet alfa) in eine Spritze des Infusionspumpensystems füllen • Für die unmittelbar anschließende **kontinuierliche Infusion 48 ml** der rekonstituierten Lösung (entspricht 480 mg Andexanet alfa) in eine Spritze des Infusionspumpensystems füllen
Niedrige Dosis	• Kurzinfusion: Volumen der Spritze mit 40 ml Infusionslösung mit einer Spritzenpumpen-Laufrate von 120 ml/h (= 15 min Dauer) intravenös infundieren • Unmittelbar anschließende kontinuierliche Infusion: Volumen der Spritze mit 48 ml Infusionslösung mit einer Spritzenpumpen-Laufrate von 24 ml/h (= 2 h Dauer) intravenös infundieren
Hohe Dosis	• Kurzinfusion: Volumen der Spritze mit 40 ml Infusionslösung mit einer Spritzenpumpen-Laufrate von 120 ml/h **zweimal hintereinander** (= 80 ml über *30 min*) intravenös infundieren • Unmittelbar anschließende kontinuierliche Infusion: Volumen der Spritze mit 48 ml Infusionslösung mit einer *Spritzenpumpen-Laufrate von 48 ml/h* **zweimal hintereinander** (= 96 ml über 2 h) intravenös infundieren

Überwachung und Beurteilung	• Baseline und Follow-up Neuroimaging (ca. 6–24 h nach Baseline) • Hämostatische Wirksamkeit (Benchmark: ≤ 35% Zunahme der Hämatomgröße von Baseline zum Follow-up Scan) • Vitalzeichen, insbesondere Blutdruck (nach Möglichkeit kontinuierliches, invasives Monitoring), relevante Neuro-Scores (während Applikation stündlich, danach zumindest alle 6 h bis zur bildgebenden und/oder klinischen Stabilisierung) • Funktionellen Status mittels mRS bei Baseline, bei Entlassung von NEIV/NEAB/NEOB, bei Entlassung aus dem Krankenhaus
Wichtiger Hinweis	• **Nach** der Gabe von **Andexanet alfa keine weitere Laborbestimmung der Anti-FXa-Aktivität**, da die Standardtestverfahren nach der Behandlung die Anti-FXa-Aktivität deutlich überschätzen • Andexanet alfa führt zu einem dosisabhängigen Anstieg der D-Dimer-Konzentration, weshalb sich dieser Parameter nicht für die Evaluierung bzgl. des Auftretens von Thrombosen eignet – In Studien waren diese D-Dimer Erhöhungen vorübergehend und bildeten sich innerhalb von 24 h bis 72 h wieder zurück

Sicherheitsüberlegungen	• Auf Anzeichen von thrombotischen Ereignissen, ischämischen Ereignissen und hämorrhagischen Ereignissen achten • Auf mögliche Infusionsreaktionen vorbereitet sein (z.B. Schüttelfrost, Kältegefühl, Bluthochdruck)
Wichtiger Hinweis	• Aufgrund der oben beschriebenen **temporären Heparin-Resistenz** soll die gleichzeitige Anwendung von unfraktoniertem Heparin und von niedermolekularen Heparinen für 24 h nach der Behandlung vermeiden werden

Nachsorge	• Start mit ***prophylaktischer*** Antikoagulation nach 24 h bei bildgebender und klinischer Stabilität • Nach Möglichkeit Erhebung des funktionellen Outcomes mittels mRS nach 90 Tagen sowie des Langzeit-Outcome nach ca. 1 Jahr (Intensivnachsorge-Ambulanz)
Wichtiger Hinweis	• Wiederaufnahme der ***therapeutischen*** Antikoagulation basierend auf individueller Risiko-Nutzen-Bewertung in Erwägung ziehen

Verantwortlichkeiten	• Neurologie: Diagnose bestätigen, Eignung feststellen, Behandlung überwachen • Pflegepersonal ZZNA/NEIV/NEAB/NEOB: Handhabung und Verabreichung von Andexanet alfa • (Neuro-) Radiologie: Interpretation der Neuroimaging-Studien

Qualitätssicherung	• Regelmäßige Überprüfung der Protokolleinhaltung und des Outcomes der Patientinnen/ Patienten • Regelmäßige Schulungen für das Personal zur Anwendung von Andexanet alfa im Kontext des ICH-Managements • Teilnahme an relevanten klinischen Registern und Studien

Literatur

Fachinformation Ondexxya 200 mg Pulver zur Herstellung einer Infusionslösung, elektronisch verfügbar unter https://enterprise.diagnosia.com/index/drug/d7e3e85caba35ce50b632835c5dfca34.pdf bzw. https://www.ema.europa.eu/de/documents/product-information/ondexxya-epar-product-information_de.pdf

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Appendix

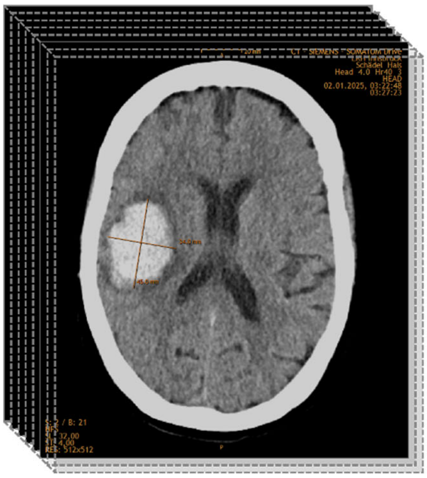
Beispiel **uHG-Kalkulation**

Synopsis (engl.) von etablierten **Neuroimaging-Parametern für die Hämatomexpansion** (Quelle: Lancet Neurol. 2023 Feb;22(2):159-171. doi: 10.1016/S1474-4422(22)00338-6)

Tabelle (engl.) **max-ICH Score** (Quelle: Neurology. 2017 Aug 1;89(5):423-431. doi: 10.1212/WNL.0000000000004174)

Auszug (engl.) **2024 AHA/ASA Performance and Quality Measures for Spontaneous Intracerebral Hemorrhage** (Quelle: Stroke. 2024 Jul;55(7):e199-e230. doi: 10.1161/STR.0000000000000464)

Appendix | Beispiel **uHG-Kalkulation**



Symptom-Onset: 02.01.2025, ca. **02:00**
Zeitpunkt Notfall-CT: 02.01.2025, **03:22**
Δt (h) = **1,33**

ICH-Volumen (sABC/2; cm³ bzw. ml) = (4,5×3,4×3,6)/2 = **27,54 ml**

uHG (ml/h) = $\frac{V}{\Delta t} = \frac{27{,}54}{1{,}33} = \mathbf{20{,}7\ ml/h}$

Appendix | Synopsis (engl.) von etablierten **Neuroimaging-Parametern für die Hämatomexpansion**

Baseline intracerebral haemorrhage volume

- There is a linear relationship between baseline volume and risk of haematoma expansion, which peaks at around 75 ml, and then declines with larger volumes.
- Easy to assess in clinical practice with the ellipsoid volume formula. For the ellipsoid volume formula, select the CT slice with the largest intracerebral haemorrhage area and measure the longest diameter (A) and the longest perpendicular diameter (B); obtain (C) by multiplying slice thickness by the number of slices in which the haematoma is detectable; intracerebral haemorrhage volume can be obtained by multiplying A × B × C and dividing by two; all measures should be taken in cm and the final volume should be reported in cm^3 or ml.
- Ultra-early haematoma growth (baseline haemorrhage volume divided by onset-to-imaging time [ml/h]) is an indirect indicator of the speed of bleeding.

CT angiography spot sign

- Presence of ≥ 1 focus of contrast extravasation within the haematoma, with any size or shape, and density more than 120 Hounsfield units (HU).
- Contrast extravasation inside the haemorrhage, with a diameter ≥ 1·5 mm, spot or serpiginous shape, no connection with vessels outside the haemorrhage, no corresponding hyperdensity on non-contrast CT, and density double than the density of the surrounding haematoma.
- Increased frequency of computed tomography angiography spot sign and diagnostic accuracy early after symptom onset.

Non-contrast CT intracerebral haemorrhage shape features

- Irregular shape: ≥ 2 margin irregularities, connected or not with the haematoma borders, and rated on the axial non-contrast CT slice with the largest haemorrhage surface.
- Island sign: ≥ 3 scattered small bleedings that are all separate from the haemorrhage or ≥ 4 small haematomas that might be connected with the main haemorrhage.
- Satellite sign: small haemorrhage (max diameter < 10 mm) that is not connected to the main haematoma, with a clear separation (1–20 mm distance).
- Subarachnoid haemorrhage: extension of parenchymal bleeding into the subarachnoid space; associated with haematoma expansion only in lobar haemorrhages.
- Satellite signs and subarachnoid haemorrhage lack external validation.

Non-contrast CT intracerebral haemorrhage density features

- Fluid level: hypoattenuating area above and hyperattenuating area below a straight line of separation (compared with the brain parenchyma); this marker lacks external validation.
- Blend sign: hypoattenuating area adjacent to a hyperattenuating area, clear margin between the two regions, and density difference greater than 18 HU.
- Black hole sign: hypoattenuating region encapsulated in the haemorrhage with a density difference > 28 HU (compared with the surrounding haemorrhage).
- Hypodensity: any hypodense region within the haemorrhage and no connection with surrounding structures; does not require density measures and can be detected with visual inspection.
- Swirl sign: any region of hypoattenuation or isoattenuation compared with the brain parenchyma, encapsulated or not in the haematoma, with any morphology.
- Heterogeneous density: ≥ 3 regions of low attenuation compared with the haemorrhage, rated on the axial slice with the largest haematoma surface.

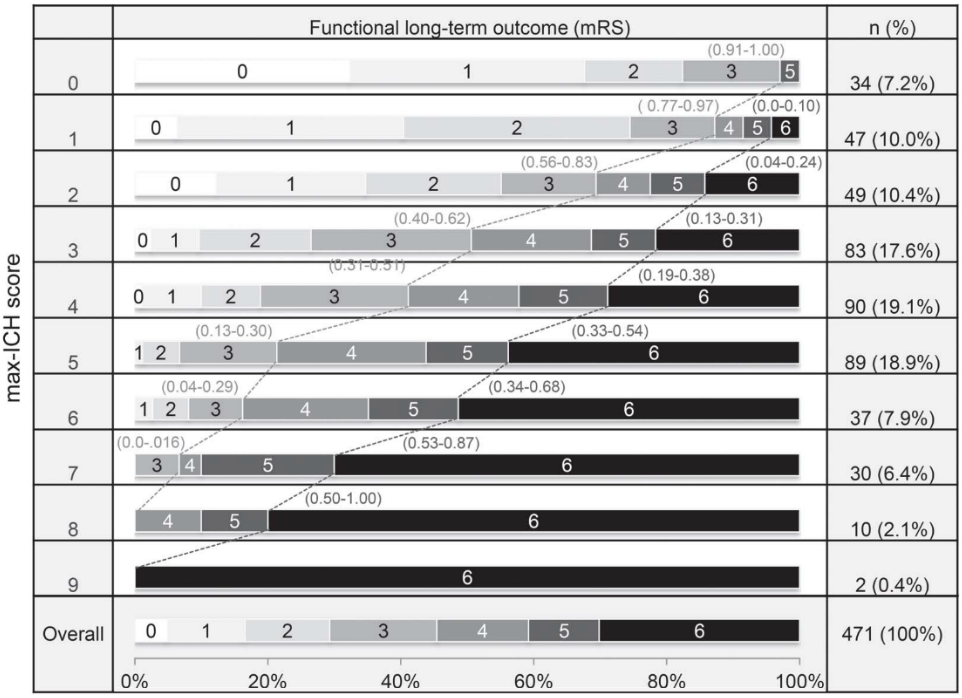
Appendix | Tabelle (engl.) **max-ICH Score**

Component	Points
NIHSS	
0–6	0
7–13	1
14–20	2
≥ 21	3
Age (yrs)	
≤ 69	0
70–74	1
75–79	2
≥ 80	3
Intraventricular hemorrhage	
No	0
Yes	1
Oral anticoagulation	
No	0
Yes	**1**
Lobar ICH volume (cm³)	
< 30	0
≥ 30	1
Nonlobar ICH volume (cm³)	
< 10	0
≥ 10	1
Total max-ICH score (0–10*)	

All components indicate measures on initial examination or initial CT/MRI. Lobar ICH was defined as ICH originating at the cortex and cortical–subcortical junction. Nonlobar ICH included deep, cerebellar, and brainstem origin. Deep ICH location was defined as ICH exclusively involving basal ganglia, thalamus, internal capsule, and deep periventricular white matter.

*ICH encompassing both deep and lobar location should be scored according to the location that ICH most likely originated from. Thus, more than 1 point referring to ICH volume can only be reached by the rare event of 2 distinct ICH (1 large lobar and 1 large nonlobar ICH).

Functional long-term outcome evaluated by modified Rankin Scale (mRS) in relation to max-ICH score classification providing point estimates for mortality and favorable functional outcome (mRS 0–3) with corresponding confidence intervals.



Stroke

PERFORMANCE AND QUALITY MEASURES

2024 AHA/ASA Performance and Quality Measures for Spontaneous Intracerebral Hemorrhage: A Report From the American Heart Association/American Stroke Association

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ABSTRACT: The American Heart Association/American Stroke Association released a revised spontaneous intracerebral hemorrhage guideline in 2022. A working group of stroke experts reviewed this guideline and identified a subset of recommendations that were deemed suitable for creating performance measures. These 15 performance measures encompass a wide spectrum of intracerebral hemorrhage patient care, from prehospital to posthospital settings, highlighting the importance of timely interventions. The measures also include 5 quality measures and address potential challenges in data collection, with the aim of future improvements.

Key Words: AHA Scientific Statements ■ cerebral hemorrhage ■ data collection ■ quality indicators, health care ■ stroke

KEY MESSAGES

- Performance measures are created as a tool to translate a subset of clinical practice guideline recommendations into evidence-based patient care to improve outcomes.
- The scope of patients with intracerebral hemorrhage in these performance measures includes patients presenting with acute, spontaneous, nontraumatic intracerebral hemorrhage without a known structural or macrovascular cause.
- The current performance measures differ from the 2018 American Heart Association/American Stroke Association Clinical Performance Measures for Adults Hospitalized With Intracerebral Hemorrhage in that they address both patients presenting to the hospital with intracerebral hemorrhage and patients who develop an acute spontaneous nontraumatic intracerebral hemorrhage during their hospitalization. In addition, measures were created to address both the prehospital and posthospital settings.
- The current document includes quality measures to address evidence-based recommendations from the 2022 guideline that have anticipated challenges with respect to feasibility of data collection and attribution. In the future, it is hoped that this will spur improved data collection and reporting so that these quality measures can be translated into performance measures.

Stroke is available at www.ahajournals.org/journal/str

Appendix 1. Performance Measurement Set Specifications

PM-1: Rapid Neuroimaging

Measure description: Percentage of patients with acute spontaneous ICH who received brain CT or MRI within 25 min of arrival to the hospital	
Numerator	Patients with acute spontaneous ICH who received brain CT or MRI within 25 min of arrival to the hospital
Denominator	All patients with acute spontaneous ICH
Denominator exclusions	Patients <18 y of age Last-known-well time >24 h before hospital arrival Clear documentation for comfort care/hospice established before hospital arrival
Denominator exceptions	Documentation of a medical reason(s) (eg, unstable for transport to neuroimaging, hemodynamic instability, need for airway management, management of agitation) Patients undergoing a noncontrast head CT in the prehospital setting (eg, in a mobile stroke unit)
Measurement period	From ED arrival until start time of initial neuroimaging
Sources of data	EHR data Administrative data/claims (inpatient claims) Administrative data/claims expanded (multiple sources) Paper medical record Radiology imaging (eg, PACS)
Attribution	Presenting facility
Care setting	Initial setting with imaging capability
Rationale	
Neuroimaging is requisite to establish the diagnosis of spontaneous ICH, which is fundamental to all subsequent aspects of care, including both medical and surgical therapies.[22,23] Neuroimaging establishes ICH size and location and distinguishes it from mimics, including ischemic stroke. The recommended time to imaging for stroke symptoms should be the same regardless of whether the final diagnosis is ischemic or hemorrhagic. We harmonized this performance measure with ischemic stroke guidelines that recommend door-to-CT time of ≤25 min. Because patients with ICH may have a higher risk of airway or hemodynamic compromise, those requiring early airway management, hemodynamic support, or management of agitation (collectively considered unstable for transport to neuroimaging) can be excluded from this measure.	
Clinical recommendation(s)	
2022 AHA/ASA management of spontaneous ICH guideline[7] 1. In patients presenting with stroke-like symptoms, rapid neuroimaging with CT or MRI is recommended to confirm the diagnosis of spontaneous ICH *(Class 1; Level of Evidence B-NR)*.	

AHA indicates American Heart Association; ASA, American Stroke Association; CT, computed tomography; ED, emergency department; EHR, electronic health record; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; and PACS, picture archiving and communication system.

CLINICAL STATEMENTS AND GUIDELINES

Appendix 1. Continued

PM-2: ICH Baseline Severity Score

Measure description: Percentage of patients with acute spontaneous ICH in whom an ICH-specific baseline severity score is measured and recorded as part of the initial hospital evaluation	
Numerator	All patients with acute spontaneous ICH in whom a baseline measure of overall hemorrhage severity is measured and a total score is recorded within 6 h of ICH diagnosis by brain CT or MRI. If an intracranial procedure is performed within 6 h of arrival, the severity score must be measured before this procedure. An ICH-specific score (eg, ICH score) should be used as the baseline measure of ICH severity. NIHSS and GCS are not sufficient to meet this performance measure.
Denominator	All patients with acute spontaneous ICH
Denominator exclusions	Patients <18 y of age Clear documentation for comfort care measures or hospice established before hospital arrival or at time of ICH diagnosis (eg, if ICH was specified as an indication to change goals of care to comfort measures in an established living will)
Denominator exceptions	
Measurement period	First 6 h after hospital arrival
Sources of data	EHR data Paper medical record Administrative data/claims (inpatient claims) Administrative data/claims expanded (multiple sources) Prospective flowsheet and retrospective medical record review
Attribution	Presenting facility and admission facility (score should be documented once within 6 h of diagnosis of ICH and does not need to be repeated by admission facility if patient has ICH score documented by presenting facility)
Care setting	Inpatient
Rationale	
Baseline clinical evaluation is part of the standard care of every patient with ICH. Using an ICH-specific severity scores that incorporates patient characteristics, anatomic location, and clinical deficit can help risk-stratify patients for ICU admission and interventions and is a primary determinant of prognosis. It also helps with assessment of disease severity, quality measures, and communication between clinicians and patients and family members.	
Clinical recommendation(s)	
2022 AHA/ASA management of spontaneous ICH guideline[7] 1. In patients with spontaneous ICH, administering a baseline measure of overall hemorrhage severity is recommended as part of the initial evaluation to provide an overall measure of clinical severity *(Class 1; Level of Evidence B-NR)*.	

AHA indicates American Heart Association; ASA, American Stroke Association; CT, computed tomography; EHR, electronic health record; GCS, Glasgow Coma Scale; ICH, intracerebral hemorrhage; ICU, intensive care unit; MRI, magnetic resonance imaging; and NIHSS, National Institutes of Health Stroke Scale.

Appendix 1. Continued

PM-3: Anticoagulant Reversal

Measure description: Percentage of patients with anticoagulant-related acute ICH who receive an appropriate reversal agent within 90 min of ED arrival along with anticoagulant discontinuation	
Numerator	Patients with anticoagulant-related acute spontaneous ICH and known or presumed current anticoagulant use* who receive an appropriate reversal agent† within 90 min of ED arrival along with anticoagulant discontinuation
Denominator	All patients with acute spontaneous ICH with known or presumed current anticoagulant use*
Denominator exclusions	Patients <18 y of age Documented allergy or contraindication to indicated reversal agent Clear documentation of comfort care or hospice before hospital arrival or at time of ICH diagnosis by brain CT or MRI (eg, if ICH was specified as an indication to change goals of care to comfort measures in an established living will) ICH due to cerebral venous sinus thrombosis Elevated INR from other cause (eg, liver disease) Hospital transfer from another facility where appropriate therapy to reverse the anticoagulant was already initiated or completed Enrolled in a clinical trial that would affect the use of anticoagulant reversal agents
Denominator exceptions	Documentation of a patient reason(s) (eg, refusal of reversal agent administration for religious or cultural reasons after demonstration of understanding of risks and benefits) Documentation of a medical reason(s) (eg, concomitant life-threatening ischemic event, ICH due to cerebral venous sinus thrombosis)
Measurement period	Initial 90 min after ED arrival
Sources of data	EHR data Administrative data/claims (inpatient claims) Administrative data/claims expanded (multiple sources) Paper medical record Pharmacy records
Attribution	Presenting facility
Care setting	Inpatient
Rationale	
Anticoagulated patients with ICH are at increased risk of HE and worse outcome compared with noncoagulopathic patients with ICH.[17,24–26] Antithrombotic reversal is associated with lower mortality and improved outcomes in VKA-associated ICH.[27,28] Because the highest-risk period for HE is the first hours after initial hemorrhage,[29–31] reversal agents should be administered as quickly as possible. Ninety min was chosen as the appropriate time period to incorporate time required for head CT and its interpretation, preparation, and administration of coagulopathy reversal.	
Clinical recommendation(s)	
2022 AHA/ASA management of spontaneous ICH guideline[7] 1. In patients with anticoagulant-associated spontaneous ICH, anticoagulation should be discontinued immediately and rapid reversal of anticoagulation should be performed as soon as possible after diagnosis of spontaneous ICH to improve survival *(Class 1; Level of Evidence C-LD).* 2. In patients with VKA-associated spontaneous ICH and INR ≥2.0, 4-factor PCC is recommended in preference to FFP to achieve rapid correction of INR and limit HE *(Class 1; Level of Evidence B-R).* 3. In patients with VKA-associated spontaneous ICH, intravenous vitamin K should be administered directly after coagulation factor replacement (PCC or other) to prevent later increase in INR and subsequent HE *(Class 1; Level of Evidence C-LD).* 4. In patients with direct factor Xa inhibitor–associated spontaneous ICH, andexanet alfa is reasonable to reverse the anticoagulant effect of factor Xa inhibitors (*Class 2a; Level of Evidence B-NR*). 5. In patients with dabigatran-associated spontaneous ICH, idarucizumab is reasonable to reverse the anticoagulant effect of dabigatran *(Class 2a; Level of Evidence B-NR).* 6. In patients with direct factor Xa inhibitor–associated spontaneous ICH, a 4-factor PCC or aPCC may be considered to improve hemostasis *(Class 2b; Level of Evidence B-NR).* 7. In patients with UFH-associated spontaneous ICH, intravenous protamine is reasonable to reverse the anticoagulant effect of heparin *(Class 2a; Level of Evidence C-LD).* 8. In patients with LMWH-associated spontaneous ICH, intravenous protamine may be considered to partially reverse the anticoagulant effect of heparin *(Class 2b; Level of Evidence C-LD).*	

AHA indicates American Heart Association; aPCC, activated prothrombin complex concentrate; ASA, American Stroke Association; CT, computed tomography; ED, emergency department; EHR, electronic health record; FFP, fresh-frozen plasma; HE, hematoma expansion; ICH, intracerebral hemorrhage; INR, international normalized ratio; LMWH, low-molecular-weight heparin; MRI, magnetic resonance imaging; PCC, prothrombin complex concentrate; UFH, unfractionated heparin; and VKA, vitamin K antagonist.

*Known or presumed current anticoagulant use at time of ICH defined as follows:

- <24 hours from last dose of oral direct factor Xa inhibitors or oral direct thrombin inhibitors
- INR ≥1.4 with VKA use
- Laboratory evidence of coagulopathy due to LMWH or heparin, (eg, elevated drug-specific anti-Xa),

†Appropriate best available reversal agents include the following:

- For oral direct factor Xa inhibitors (eg, apixaban, rivaroxaban, edoxaban) taken within 24 hours* of ED arrival OR if time of last dose unknown OR elevated drug-specific activity level: andexanet alpha OR 4-factor PCC OR aPCC
- For oral direct thrombin inhibitors (eg, dabigatran) taken within 24 hours* of ED arrival OR if time of last dose unknown OR elevated drug specific activity level: idarucizumab OR PCC or aPCC and/or renal replacement therapy
- For UFH and LMWH with elevated drug-specific anti-Xa level: protamine
- For VKA with an INR ≥1.4: 4-factor PCC with intravenous vitamin K.

Appendix 2. Continued

QM-4: Time to BP Target

Measure description: Percentage of patients with acute spontaneous ICH in whom acute BP lowering is initiated within 1 h of hospital arrival and in whom the target BP is reached within 2 h of hospital arrival	
Numerator	Patients with acute spontaneous ICH in whom pharmacological BP lowering is initiated within 1 h of hospital arrival and with the target BP reached within 2 h of hospital arrival
Denominator	All patients with acute spontaneous ICH in whom BP lowering is initiated
Denominator exclusions	Patients <18 or ≥90 y of age Presenting systolic BP <150 or >220 mm Hg Initial GCS score <5 Hematoma volume ≥60 mL[3] Patients transferred from another hospital (Note: First 4 exclusions derive from the ATACH-2 clinical trial[77] from which the data for the AHA ICH guideline recommendation are derived)
Denominator exceptions	Documentation of a medical reason(s) (eg, enrollment in clinical trial specifying BP management, documentation of medical reason why BP lowering should not be initiated)
Measurement period	Encounter
Sources of data	EHR data Paper medical record
Attribution	Admission facility
Care setting	Inpatient
Rationale	
The purpose of this measure would be to encourage rapid but controlled BP lowering in patients with ICH. The text from the 2022 ICH guidelines[7] indicates that the data from 2 h of onset come from a post hoc substudy of a single clinical trial (ATACH-2)[77] and does not provide supporting text for meeting the 1-h postinitiation target. It also does not provide a specific target because the ATACH-2 trial tested 2 different targets and did not find a difference in outcome between these 2 targets. Although time from ICH onset is often not under the control of hospitals and clinicians who receive patients as a primary destination or in transfer, time from arrival to treatment is. Thus, a 60-min window to initiation of BP lowering is used analogous to a door-to-needle time for AIS. Sixty min also allows a slow and steady reduction in BP to reduce large variability, which can worsen functional outcomes in patients with ICH. A specific BP target is not included in this measure. To meet this measure, a hospital must specify a target in the individual patient and meet this patient-specific target.	
Clinical recommendation(s)	
2022 AHA/ASA management of spontaneous ICH guideline[7] 1. In patients with spontaneous ICH in whom acute BP lowering is considered, initiating treatment within 2 h of ICH onset and reaching target within 1 h can be beneficial to reduce the risk of HE and improve functional outcome *(Class 2a; Level of Evidence C-LD).* 2. In patients with spontaneous ICH requiring acute BP lowering, careful titration to ensure continuous smooth and sustained control of BP, avoiding peaks and large variability in SBP, can be beneficial for improving functional outcomes (*Class 2a; Level of Evidence B-NR*).	

AHA indicates American Heart Association; AIS, acute ischemic stroke; ASA, American Stroke Association; ATACH-2, Antihypertensive Treatment of Acute Cerebral Hemorrhage II; BP, blood pressure; EHR, electronic health record; GCS, Glasgow Coma Scale; HE, hematoma expansion; ICH, intracerebral hemorrhage; and SBP, systolic blood pressure.