DCI RESCUE PATHWAY — INDUCED HYPERTENSION + ADJUNCTIVE MILRINONE

For Delayed Cerebral Ischemia after Aneurysmal Subarachnoid Hemorrhage

Citations in gray italics reference the numbered source list at the end of the document.

1. Background and treatment philosophy

Delayed cerebral ischemia (DCI) is the leading preventable cause of morbidity after aneurysmal subarachnoid hemorrhage (aSAH). It occurs in approximately one-third of patients, peaks between days 4 and 14 post-bleed, and is responsible for significant long-term disability. The pathophysiology is multifactorial — large-vessel vasospasm contributes but does not fully explain the syndrome; microcirculatory dysfunction, cortical spreading depolarization, and neuroinflammation also play a role. *[Ref 2, 13, 14, 15]*

This protocol reflects a staged treatment strategy:

1. First-line: Induced hypertension (IH) using norepinephrine to restore cerebral perfusion in the face of symptomatic vasospasm. Norepinephrine is the preferred first agent based on its balanced α/β activity, lower risk of tachycardia than phenylephrine, and a favorable comparative safety profile. *[Ref 14, 15, 23, 24]*
2. Second-line adjunct: IV milrinone infusion when IH alone is inadequate (persistent neurologic deficit despite achieved BP goal, or worsening transcranial Doppler velocities). Milrinone provides cerebral microcirculatory vasodilation and inotropic support. *[Ref 1, 2, 3, 4]*
3. Rescue: Intra-arterial (IA) verapamil ± mechanical angioplasty, performed by interventional neuroradiology, for refractory DCI despite maximal medical therapy. *[Ref 25, 26]*

Important framing: The blood pressure target in this protocol is a FLOOR (goal to achieve), not a ceiling. The pressor team is responsible for BP augmentation. Milrinone is not intended to raise BP; it is a vasodilator/inotrope added to improve cerebral microcirculation when IH alone is insufficient.

Evidence caveat: Induced hypertension for DCI is supported by large observational series but the only randomized trial (HIMALAIA, Gathier 2018) was halted early for ineffectiveness and slow recruitment. IV milrinone is off-label and supported by observational studies including the MILRISPASM controlled before-after study (2021); the confirmatory MiVAR RCT is ongoing. Both the 2023 AHA/ASA and 2023 Neurocritical Care Society aSAH guidelines describe the evidence base as limited. *[Ref 3, 14, 15, 17]*

2. Indications to activate the DCI Rescue pathway

Activate this pathway when ALL of the following are met:

1. Confirmed aSAH with secured aneurysm (coiling or clipping documented). *[Ref 14, 15]*
2. New symptoms consistent with DCI as defined by Vergouwen consensus criteria: a new focal neurologic deficit (hemiparesis, aphasia, apraxia, hemianopia, neglect) OR a decrease in GCS of ≥2 points (total or sub-score) lasting ≥1 hour, not apparent immediately after aneurysm occlusion, and not attributable to another cause after imaging/laboratory workup. *[Ref 13]*
3. Typically days 4–14 post-bleed (peak vasospasm window), though DCI can occur outside this window. *[Ref 1, 2]*
4. Radiographic evidence of vasospasm where feasible: CT angiography, digital subtraction angiography, OR transcranial Doppler (elevated mean MCA velocity with Lindegaard ratio supporting vasospasm over hyperemia). *[Ref 2]*

Oral nimodipine 60 mg PO/NG every 4 hours × 21 days is a foundational therapy and should already be ordered on day 1; it must continue throughout DCI treatment.

3. Absolute contraindications (hard stops)

The following are absolute contraindications that block order entry. Other relative cautions (CAD, reduced LVEF, CrCl <30, pulmonary edema) are addressed by clinical judgment and surfaced as prescriber reminders, not gates.

Contraindication	Impact on pathway	Source
Unsecured ruptured aneurysm	Blocks the entire pathway. Induced hypertension before aneurysm securement carries unacceptable rebleed risk.	*[Ref 14, 15]*
Severe aortic stenosis, severe mitral stenosis, or hypertrophic obstructive cardiomyopathy (HOCM)	Blocks the milrinone sub-section. Induced hypertension alone may still be acceptable with cardiology input. Milrinone's afterload reduction is poorly tolerated with fixed LV outflow obstruction.	*[Ref 2, 22]*

Prescriber reminders (surfaced in the order set but not blocking)

- CrCl <30 mL/min: published milrinone DCI protocols exclude this group; pharmacy review required before adding milrinone. *[Ref 2, 21]*
- LVEF <35%, recent MI, or significant CAD: induced hypertension increases myocardial oxygen demand; consider cardiology consult. Troponin rise occurs in ~10–17% of IH-treated patients. *[Ref 17, 27]*
- Platelet count <100 × 10^9/L: relative caution for milrinone. *[Ref 2]*
- Patient must be in neuro-ICU with continuous arterial BP, continuous ECG, and 1:1 or 1:2 nursing.

4. Hemodynamic goals (prescriber-selected at order entry)

SBP floor — primary BP goal

Three tiers are available at order entry. The nurse titrates pressors to maintain SBP AT OR ABOVE the selected floor while the neurologic deficit persists.

Tier	SBP floor	Use case	Source
Conservative	**SBP ≥ 160 mmHg**	Cardiac risk factors, prior MI, elderly (>75), borderline hemodynamic tolerance.	*[Ref 14, 23]*
Standard (default)	**SBP ≥ 180 mmHg**	Most DCI patients. Published IH series target SBP 160–230 mmHg; 180 sits near the midpoint and is the most commonly used default.	*[Ref 23, 24]*
Aggressive	**SBP ≥ 200 mmHg**	Refractory DCI or poor-grade SAH with active deficit unresponsive to lower tiers. Attending neurointensivist discussion documented.	*[Ref 23, 24]*

Absolute upper safety cap: SBP 220 mmHg. *Above this level, slow the pressor and notify MD regardless of selected tier. This matches the pragmatic upper cap used in the Dutch IH cohort.* *[Ref 24]*

MAP floor — secondary BP goal

At order entry, prescriber selects MAP floor from: 90, 100, 110, or 120 mmHg. Default selection should correlate with the SBP tier (higher SBP floor pairs with higher MAP floor).

MAP floor option	Typical pairing	Clinical scenario	Source
MAP ≥ 90 mmHg	Conservative SBP ≥ 160	Cardiac caution	*[Ref 1, 2]*
MAP ≥ 100 mmHg	Standard SBP ≥ 180	Default	*[Ref 3, 23]*
MAP ≥ 110 mmHg	Aggressive SBP ≥ 200	Refractory DCI	*[Ref 23]*
MAP ≥ 120 mmHg	Aggressive + escalation	Attending-directed only	*[Ref 23]*

The nurse maintains BOTH SBP ≥ floor AND MAP ≥ floor. Both values appear on the MAR as the titration target.

5. Vasopressor cascade and fluids

Pressors are escalated sequentially, not titrated against each other. Each is added when the previous is at or near its ceiling without achieving the BP goal.

First-line: norepinephrine

- **Starting rate:** 0.05 mcg/kg/min.
- **Titration:** increase by 0.02–0.05 mcg/kg/min every 3–5 minutes until SBP and MAP floors are met. *[Ref 14]*
- **Ceiling:** 1.5 mcg/kg/min. Above this, add second-line agent. *[Ref 3]*
- **Rationale for first-line use:** balanced α1/β1 activity preserves cardiac output while raising systemic vascular resistance. Compared to phenylephrine, norepinephrine is associated with lower risk of reflex bradycardia, less myocardial ischemia, and possibly lower mortality in aSAH cohorts. *[Ref 14, 23, 24]*

Second-line: phenylephrine

- **Indication:** add when norepinephrine titration is limited by tachycardia (HR >130) or new arrhythmia, OR as an alternative first-line agent when the attending judges pure α activity is preferable (severe CAD, active tachyarrhythmia). *[Ref 24]*
- **Starting rate:** 0.5 mcg/kg/min.
- **Titration range:** 0.25–5 mcg/kg/min.
- **Caution:** phenylephrine is associated with higher rates of ECG changes and troponin elevation than norepinephrine in IH cohorts; monitor closely. *[Ref 17, 27]*

Third-line: vasopressin

- **Indication:** add when norepinephrine ≥0.5 mcg/kg/min (± phenylephrine) is unable to achieve SBP floor. *[Ref 28]*
- **Dose:** 0.03 units/min, FIXED (not titrated).
- **Caution:** vasopressin is associated with hyponatremia in SAH; monitor sodium closely. Some institutions avoid it in SAH for this reason. *[Ref 28]*

Fluids

- **Baseline:** 0.9% NaCl at 75 mL/hr continuous maintenance.
- **Goal:** euvolemia. Do NOT provide hypervolemia — the 2023 AHA/ASA and NCS guidelines recommend AGAINST hypervolemia/triple-H therapy based on lack of benefit and pulmonary edema risk. *[Ref 14, 15]*
- **PRN boluses:** use sparingly and only for documented volume depletion. A routine PRN bolus order is NOT included in this pathway.

6. Milrinone — second-line adjunct

When to add milrinone

Milrinone is added — not substituted — when IH alone is inadequate. Specific triggers:

- Persistent or worsening neurologic deficit despite SBP and MAP at goal on norepinephrine ± phenylephrine. *[Ref 2, 3, 4]*
- Worsening TCD mean velocities or Lindegaard ratio despite IH at goal. *[Ref 2]*
- Inability to tolerate further pressor escalation due to tachyarrhythmia or myocardial strain, with persistent deficit. *[Ref 3]*

Milrinone is NOT a first-line substitute for induced hypertension. It is a vasodilator and will not raise BP.

Milrinone dosing

Parameter	Value	Source
Concentration	200 mcg/mL (20 mg in 100 mL 0.9% NaCl or D5W)	*[Ref 22]*
Loading bolus	OMIT at initiation. (A 50 mcg/kg bolus over 10 min may be ordered separately for weaning-phase symptom recurrence only, and only with SBP ≥100 mmHg pre-bolus.)	*[Ref 2, 19, 20]*
Starting dose	**0.5 mcg/kg/min**	*[Ref 3]*
Titration step	Increase by 0.25 mcg/kg/min every 1–2 hours if deficit unchanged/worsening AND no trigger below is met	*[Ref 2]*
Nurse-driven maximum	**1.5 mcg/kg/min**	*[Ref 3]*
Above-ceiling escalation	Requires new MD order, attending approval, AND interventional neuroradiology consult for IA rescue consideration	*[Ref 2, 4]*

Parameter	Value	Source
Renal adjustment	CrCl 40–50: start 0.43; CrCl 30–40: start 0.33; CrCl <30: attending + pharmacy review required	*[Ref 2, 22]*
Line	Dedicated central lumen preferred; peripheral acceptable ≤4 hr as bridge to central access	

Baseline values captured at order entry

The following are captured at the time milrinone is ordered and anchor the trigger logic below:

- Baseline HR (pre-milrinone): anchors the HR rise trigger.
- Pre-milrinone SBP: documented for reference but NOT used as a trigger (pressor team handles BP).

7. Milrinone titration triggers (nurse-driven)

The following table governs nurse-driven titration of milrinone. The SBP floor is handled by the pressor team; milrinone's triggers are focused on adverse effects and the pressor team's ability to maintain the BP goal.

Trigger	Action	Source
Unable to maintain SBP ≥ [floor] despite norepinephrine at 1.5 mcg/kg/min	FAILED milrinone tolerance. Do NOT increase or decrease milrinone — MAINTAIN current dose. Escalate pressor support (add phenylephrine, then vasopressin). Notify neurointensivist attending.	*[Ref 3]*
HR >100 bpm AND increase >20 bpm from baseline (captured at order entry)	Do NOT up-titrate. Check K^+ and Mg^{2+}, replace per protocol. If HR remains elevated after electrolytes corrected and sustained >15 min, notify MD.	*[Ref 3, 20]*
Dose reaches 1.5 mcg/kg/min	Maximum nurse-driven dose. Any further escalation requires new MD order, attending approval, AND IR consult.	*[Ref 2, 3, 4]*
New atrial fibrillation, ventricular arrhythmia, troponin rise, or platelets <100 × 10^9/L	HOLD milrinone. Notify MD immediately. 12-lead ECG, repeat troponin, electrolyte check.	*[Ref 2, 20]*
Polyuria >250 mL/hr × 2 hr with hemodynamic instability	Replace K^+ and Mg^{2+} empirically per §11. Do NOT fluid restrict. Notify MD if instability persists.	*[Ref 3, 21]*

Trigger	Action	Source
Neurologic deficit WORSENS despite milrinone at 1.5 mcg/kg/min AND max pressor support	Notify attending immediately. Request IR consult for IA verapamil ± angioplasty. Prepare patient for possible transport.	*[Ref 2, 4, 25, 26]*
STOP criteria: VT/VF, MAP <65 mmHg despite max pressors, acute MI, anaphylaxis, acute non-DCI neuro deterioration (rebleed, hydrocephalus, seizure)	STOP milrinone immediately. Notify MD. Evaluate for cause.	

8. Bedside nursing workflow summary

On initiation

1. Confirm hard stops passed and MD orders signed.
2. Confirm arterial line, continuous ECG, central IV access preferred.
3. Start norepinephrine at 0.05 mcg/kg/min. Titrate q3–5 min to SBP and MAP floors.
4. If SBP floor not achieved at norepinephrine 1.5 mcg/kg/min, add phenylephrine per order.
5. If still not achieved, add vasopressin 0.03 units/min per order. Notify MD.
6. If milrinone is ordered: start at 0.5 mcg/kg/min, document baseline HR on MAR.
7. Baseline neurologic exam documented.

During titration

- **Reassess neurologic exam:** every 30 minutes during active titration.
- **Vital signs:** continuous BP, HR, rhythm; document q15 min after any change.
- **Up-titrate milrinone** by 0.25 mcg/kg/min every 1–2 hours if deficit unchanged or worsening AND no trigger met (see §7). *[Ref 2]*
- **Do NOT titrate milrinone** in response to BP — that is the pressor team's role.

Once goals met AND deficit improving

- Maintain current pressor and milrinone doses.
- Reassess neurologic exam hourly for 12 hours, then q2h.
- Continue TCD daily.

9. Escalation to interventional neuroradiology

IA rescue (verapamil ± mechanical angioplasty) is prescriber-driven, not auto-triggered. Consider IR consult when:

- Persistent or worsening focal deficit despite IH (norepinephrine ≥1.5 mcg/kg/min ± phenylephrine) PLUS milrinone at 1.5 mcg/kg/min. *[Ref 2, 4]*

- Persistently elevated or worsening TCD velocities despite maximal medical therapy. *[Ref 2]*
- CTA or DSA evidence of severe angiographic vasospasm (>50% narrowing) with corresponding clinical deficit. *[Ref 2, 25]*
- Patient unable to tolerate maximal medical therapy due to hemodynamic or cardiac intolerance. *[Ref 3]*

Evidence for IA rescue options

IA verapamil at 10 ± 3 mg per arterial distribution (or higher doses in experienced centers) improves angiographic vessel diameter and has documented clinical improvement in ~74% of treated patients in large cohorts. Effect is transient (hours), repeated treatments may be required. *[Ref 25, 26]*

Mechanical angioplasty provides durable dilation of proximal cerebral vessels but carries rupture risk (~1%) and is limited to accessible segments (typically proximal MCA, distal ICA, basilar). Distal or diffuse vasospasm is better suited to IA vasodilators. *[Ref 25]*

The interventional neuroradiology team makes the final decision on IA verapamil vs. mechanical angioplasty based on angiographic findings in the suite.

10. Monitoring requirements

Parameter	Frequency / target	Source
Arterial BP, HR, rhythm, SpO_2	Continuous. Arterial line required.	*[Ref 2]*
Neurologic exam	Every 30 min during active titration; hourly × 12 hr after stabilization; then q2h while on IH/milrinone	*[Ref 1, 2]*
Intake / output	Hourly. Flag urine output >250 mL/hr × 2 hours.	*[Ref 3]*
BMP, Mg^{2+}, phosphate	q6h × 24h, then q12h. Targets: K^+ ≥4.0 mmol/L; Mg^{2+} ≥2.0 mg/dL.	*[Ref 3]*
CBC with platelets	Daily	*[Ref 2]*
Troponin	Baseline; repeat if new ECG change, chest pain, arrhythmia, or MAP >20 mmHg above baseline. Troponin rise is reported in ~10–17% of IH-treated patients.	*[Ref 17, 27]*
12-lead ECG	Baseline, daily, and after milrinone escalation >1.0 mcg/kg/min or any new rhythm change	*[Ref 2]*
Transcranial Doppler	Daily. Trend mean MCA velocity and Lindegaard ratio. Escalating velocities with clinical correlate ⟶ IR consult.	*[Ref 2]*
Sodium (if on vasopressin)	q6h while on vasopressin. Vasopressin risk of hyponatremia is significant in SAH.	*[Ref 28]*
Temperature, glucose, ICP	Per institutional SAH protocols. Normothermia, glucose 140–180.	*[Ref 14, 15]*

11. Standing electrolyte replacement

Polyuria from augmented renal clearance is common; median CrCl in MILRISPASM milrinone-treated patients was 191 mL/min. Aggressive empiric replacement reduces arrhythmia risk. *[Ref 3, 21]*

Electrolyte	Trigger	Replacement (adult, normal renal function)	Source
Potassium	K^+ 3.5–3.9	KCl 40 mEq IV or PO — recheck in 4 hours	*[Ref 3]*
Potassium	K^+ 3.0–3.4	KCl 60 mEq IV — recheck in 2 hours	*[Ref 3]*
Potassium	K^+ <3.0	Notify MD; hold milrinone up-titration; KCl per MD with continuous telemetry	*[Ref 3]*
Magnesium	Mg^{2+} 1.8–1.9 mg/dL	$MgSO_4$ 2 g IV over 1 hour	*[Ref 14]*
Magnesium	Mg^{2+} <1.8 mg/dL	$MgSO_4$ 4 g IV over 2 hours; recheck in 4 hours	*[Ref 14]*
Phosphate	PO_4 <2.0 mg/dL	KPhos or NaPhos per renal pharmacy guidance	
Sodium	Na^+ <135 or trending down	Notify MD. Do NOT fluid-restrict. Consider isotonic or hypertonic saline per MD. Cerebral salt wasting common in SAH; vasopressin compounds risk.	*[Ref 14, 28]*

12. De-escalation and weaning

The pathway is de-escalated in reverse order: milrinone first, then pressors, then monitoring level. Do NOT wean more than one therapy at a time.

Phase 0 — Eligibility (assess daily)

Patient must meet ALL of the following before de-escalation begins:

1. No new DCI symptoms for 72 consecutive hours. *[Ref 1, 2]*
2. TCD mean velocities stable or trending down × 2 consecutive studies. *[Ref 2]*
3. If follow-up CTA/DSA was performed, no new or worsening vasospasm.
4. Days 10–14 post-bleed reached, OR beyond the peak vasospasm window for this patient per attending. *[Ref 1, 9]*
5. Hemodynamically stable on current milrinone dose.
6. No active electrolyte derangement (K^+ ≥4.0, Mg^{2+} ≥2.0).
7. Attending physician order to initiate de-escalation documented.

Phase 1 — Wean milrinone

- **Rate:** decrease by 0.25 mcg/kg/min every 24 hours. *[Ref 1, 2]*

- **Timing:** perform step-downs in the morning for full awake-team observation.
- **Reassessment:** neurologic exam at 30 min, 1 hr, 2 hr, 4 hr, 8 hr after each step.
- **Discontinue:** at 0.25 mcg/kg/min if asymptomatic × 24 hr. Do NOT leave patient on 0.25 indefinitely. *[Ref 2]*

Phase 2 — Wean pressors

- **Begin only after milrinone has been off ≥12 hours AND patient remains asymptomatic.**
- **Wean vasopressin first, then phenylephrine, then norepinephrine.**
- **Norepinephrine decrements:** 0.02–0.05 mcg/kg/min every 2–4 hours as MAP tolerates, targeting baseline (pre-DCI) MAP. *[Ref 14, 15]*
- **Stop immediately** if any new focal deficit, GCS drop ≥2, or TCD worsening.

Phase 3 — De-escalate monitoring

- Continue TCD daily for ≥48 hours after all vasoactive agents off. *[Ref 2]*
- Continue arterial line and continuous telemetry ≥24 hours after all vasoactives off.
- Continue nimodipine for the full 21-day course. *[Ref 14, 15]*

Phase 4 — Transfer readiness

Ward transfer when ALL met for ≥24 hours:

- Off milrinone and all pressors.
- Stable neurologic exam.
- TCD stable or improved × last 2 studies.
- Beyond day 14 post-bleed. *[Ref 9]*

Recurrence during de-escalation

If new DCI symptoms emerge at ANY phase:

1. Stop active weaning immediately.
2. Return milrinone (if previously discontinued, restart at last effective dose); reinstate any weaned pressor. *[Ref 1, 2]*
3. Notify attending. Consider urgent CTA/DSA to assess vasospasm and rule out new infarction.
4. Hold all further weaning ≥24 hours after symptom resolution. *[Ref 2]*
5. The 72-hour symptom-free window (Phase 0) must be re-established before de-escalation resumes. *[Ref 1, 2]*

Typical duration

IH therapy: 3–7 days in most cohorts (Dutch series used a 3-day taper if clinical response occurred). **Milrinone: 5–14 days** *(mean 9.8 days in the Montreal series), corresponding to the peak vasospasm window.* *[Ref 1, 24]*

13. Documentation requirements

Document in the EMR flowsheet / MAR at minimum:

- Each pressor or milrinone dose change: time, old rate, new rate, reason, MD notified Y/N
- Vital signs before and 30/60 min after each change
- Neurologic exam before and after each change
- Hourly I&O and cumulative balance
- All electrolyte replacements given
- TCD findings reviewed with MD
- De-escalation phase (0/1/2/3/4) at shift change
- Any failed-pressor-tolerance event (inability to reach SBP floor) with timestamp and dose reached

14. Quality metrics (track quarterly)

- Time from DCI diagnosis to achievement of SBP goal
- Time from DCI diagnosis to milrinone initiation (when used)
- Incidence of SBP goal NOT achieved despite triple pressor therapy
- Incidence of troponin elevation or new ECG changes during IH
- Incidence of new atrial fibrillation on pathway
- Percentage of milrinone discontinuations for hemodynamic intolerance
- Percentage of pathway activations proceeding to IA rescue
- Percentage of de-escalations requiring return to previous phase
- 6-month mRS when obtainable
- Protocol deviations with root-cause review

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Inline citations throughout the protocol refer to the numbered sources below.

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