

AMI with Heart Failure for the Acute Care, Emergency and Critical care Physician in ICU— updated to the 2026 ESC Heart Failure Guidelines

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About this draft- How to introduce 4 pillars of management

FMT- Foundational Medical therapy

AMT- Additional Medical therapy

GDMT- Guideline Directed medical therapy

- **Terminology note:** after AMI, “preserved LVEF” ($\geq 50\%$) is not the same as HFpEF. HFpEF requires a heart failure syndrome; most patients in REDUCE-AMI and REBOOT had no HF. The draft uses “preserved LVEF” where that is what the trials enrolled.

A. Beta-blockers in recent AMI with heart failure

Beta-blockers are firmly indicated after AMI when LVEF is $\leq 40\%$; for LVEF 41–49% the 2025 pooled data now show benefit, and for LVEF $\geq 50\%$ without another indication they show none.

Question 1: What is the indication for beta-blocker therapy after AMI based on LVEF?

Answer: Beta-blocker therapy is indicated for long-term use following an AMI primarily in patients with heart failure with reduced ejection fraction (HFrEF, LVEF $\leq 40\%$) or heart failure with mildly reduced ejection fraction (HFmrEF, LVEF 41–49%).

- **HFrEF (LVEF $\leq 40\%$):** Class I, Level of Evidence A recommendation. Beta-blockers improve survival, prevent adverse remodelling, and reduce re-infarction and sudden cardiac death.
- **HFmrEF (LVEF 41–49%):** Class IIa recommendation. Evidence demonstrates a significant reduction in major adverse cardiovascular events (MACE) and re-infarction.
- **HFpEF (LVEF $\geq 50\%$):** Routine long-term beta-blockers are not indicated solely for post-AMI prophylaxis in contemporary reperfused patients unless secondary indications exist (e.g., angina, atrial fibrillation, uncontrolled hypertension).

Question 2: What is the optimal starting time for beta-blocker initiation after an AMI?

Answer: Beta-blockers should be initiated orally within 24 hours of AMI presentation, provided the patient is haemodynamically stable and free from clinical signs of acute decompensated heart failure or cardiogenic shock.

- **Stability criteria for early start:** Absence of Killip class III/IV signs (pulmonary oedema, hypotension with SBP < 100 mmHg, bradycardia HR < 50 bpm, or high-degree AV block).
- **If acute decompensation / low output is present:** Delay initiation until haemodynamic stability is achieved, volume status is optimised, and intravenous inotropes (if any) are stopped.

- **Avoid routine IV beta-blockers:** Intravenous beta-blocker boluses should be avoided during acute STEMI/NSTEMI presentations due to an increased risk of cardiogenic shock (demonstrated in COMMIT/CCS-2).

Question 3: Which beta-blockers are evidence-based for post-AMI patients with reduced EF, and what are their dosing and titration protocols?

Answer: Only four specific evidence-based beta-blockers are recommended for heart failure and post-AMI systolic dysfunction. Dosing must follow a “start low, go slow” strategy, titrating every 2–4 weeks toward landmark trial target doses.

Beta-blocker	Starting dose	Target dose	Key properties
Carvedilol	3.125 mg BID	25 mg BID (50 mg BID if >85 kg)	Non-selective β_1 , β_2 + α_1 -blocker (vasodilatory, reduces afterload)
Metoprolol succinate (CR/XL)	12.5–25 mg once daily	200 mg once daily	Selective β_1 -blocker (extended-release formulation only)
Bisoprolol	1.25 mg once daily	10 mg once daily	Highly selective β_1 -blocker
Nebivolol	1.25 mg once daily	10 mg once daily	Selective β_1 -blocker with nitric-oxide-mediated vasodilation (SENIORS trial)

Question 4: How should beta-blocker doses be adjusted in response to adverse effects or clinical instability?

Answer:

- **Symptomatic bradycardia (HR <50 bpm) or heart block:** Reduce the dose by 50% or hold temporarily. Evaluate for drug interactions (e.g., non-dihydropyridine CCBs, digoxin, amiodarone).
- **Symptomatic hypotension (SBP <90 mmHg):** First stagger dosing relative to ACEi/ARNI or nitrates. If symptoms persist without systemic congestion, reduce the beta-blocker dose.
- **Mild fluid retention / mild HF worsening:** Increase diuretics first before reducing the beta-blocker dose.
- **Severe decompensated HF / cardiogenic shock:** Temporarily lower or hold the beta-blocker, manage congestion/perfusion, and re-initiate at a lower dose before hospital discharge.
- **Sudden withdrawal warning:** Never stop beta-blocker therapy abruptly in stable patients; abrupt cessation can precipitate rebound ischaemia, ventricular arrhythmias, or recurrent infarction.

Question 5: What is the trial evidence supporting beta-blockers in post-AMI patients with HFrEF?

1. CAPRICORN (Carvedilol Post-Infarct Survival Control in LV Dysfunction)

- **P:** 1,959 patients post-AMI with LV dysfunction (LVEF $\leq$ 40%) receiving modern background therapy (ACE inhibitors).
- **I:** Carvedilol titrated up to 25 mg BID.
- **C:** Placebo.
- **O:** **23% reduction in all-cause mortality** (HR 0.77, $p=0.031$) and 40% reduction in recurrent non-fatal MI (HR 0.60, $p=0.011$).

2. MERIT-HF (Metoprolol CR/XL Randomised Intervention Trial in Heart Failure)

- **P:** 3,991 patients with symptomatic HF (LVEF $\leq 40\%$), including post-MI subgroup.
- **I:** Metoprolol succinate CR/XL titrated up to 200 mg once daily.
- **C:** Placebo.
- **O:** 34% reduction in all-cause mortality (HR 0.66, $p=0.00009$) and a 41% reduction in sudden cardiac death.

Question 6: What is the trial evidence for beta-blockers in post-AMI patients with preserved or mildly reduced EF?

1. REDUCE-AMI (2024)

- **P:** 5,020 post-AMI patients with preserved LVEF ($\geq 50\%$) managed with an invasive strategy (PCI) and medical therapy.
- **I:** Long-term beta-blocker therapy (metoprolol or bisoprolol).
- **C:** No beta-blocker therapy.
- **O:** No significant difference in the composite of death or recurrent MI (HR 0.96, $p=0.64$).

2. REBOOT & BETAMI-DANBLOCK trials and pooled meta-analyses (2025–2026)

- **P:** Patients undergoing reperfusion for AMI with LVEF $>40\%$ (divided into LVEF 41–49% and $\geq 50\%$).
- **I:** Beta-blocker administration.
- **C:** Standard care without beta-blockers / discontinuation.
- **O:** In LVEF 41–49%, significant reduction in the composite endpoint (HR 0.73, $p=0.037$). In LVEF $\geq 50\%$, no mortality or MACE reduction.

Study	Population	Result
REBOOT [11]	8,505; LVEF $>40\%$, no HF	Death, re-MI or HF admission: HR 1.04 (0.89–1.22), $p=0.63$ — no benefit
BETAMI-DANBLOCK [12]	5,574; LVEF $\geq 40\%$, no HF	Death or MACE: 14.2% vs 16.3% — significant benefit, driven by fewer re-infarctions
IPD meta-analysis, LVEF 40–49% [13]	1,885	HR 0.75 (0.58–0.97), $p=0.031$ — benefit
IPD meta-analysis, LVEF $\geq 50\%$ [14]	17,801	HR 0.97 (0.87–1.07), $p=0.54$ — no benefit

The two 2025 trials disagreed overall: REBOOT was neutral and BETAMI-DANBLOCK positive. The source's HR 0.73/ $p=0.037$ does not match any published figure.

Summary of timing and agent selection in key post-AMI beta-blocker trials

1. CAPRICORN (HFrEF): Carvedilol, started at 6.25 mg BID and titrated to 25 mg BID. Enrolment window 3–21 days post-AMI; mean start about 10 days, after ACE inhibitor for at least 48 hours.

2. REDUCE-AMI (LVEF $\geq 50\%$): Metoprolol succinate or bisoprolol, chosen by local practice. Enrolment 1–7 days post-AMI; median start 1–3 days (in hospital, post-PCI).

3. REBOOT (LVEF $>40\%$): Pragmatic clinician choice; bisoprolol predominant ($>85\%$), with metoprolol, carvedilol and nebivolol for the rest. Enrolment at discharge or up to 14 days; median start 3–5 days.

4. BETAMI-DANBLOCK (LVEF $>40\%$): Metoprolol or bisoprolol. Enrolment within 14 days; median start **2–4** days.

Clinical takeaways across trials (from source): Historical reduced-EF trials used carvedilol; contemporary reperfusion-era trials used cardioselective β 1-blockers. Early trials waited 1–2 weeks; modern trials randomised within 1–5 days, usually during the index admission after PCI.

Take-home message — Beta-blockers: Start an evidence-based oral beta-blocker (bisoprolol, carvedilol or metoprolol succinate) within 24 hours once the patient is out of pulmonary oedema and shock, and titrate every 2–4 weeks. LVEF $\leq 40\%$: mandatory. LVEF 40–49%: now supported by pooled RCT data. LVEF $\geq 50\%$ with no angina, arrhythmia or hypertension: no proven benefit — reassess the need at follow-up. **No IV beta-blockers in HF or shock.**

2026 ESC update — beta-blockers [36]

Setting	2026 status	Class / level
Symptomatic HFrEF (now LVEF $< 50\%$)	FMT	Class I
Stage B, LVEF $< 50\%$ (includes post-MI 41–49% without HF)	Recommended to reduce HF hospitalisation or death	I B1
Post-MI, LVEF $> 50\%$, no other indication	Guideline text argues against routine use (REDUCE-AMI, REBOOT, BETAMI-DANBLOCK)	No recommendation
HFpEF ($\geq 50\%$)	Not FMT	—
HFrEF with atrial fibrillation (stable)	First-line rate control	I C
Advanced HFrEF with organ hypoperfusion	Down-titrate or stop	IIa C
Pregnancy with HFrEF	Switch non-selective to β 1-selective (metoprolol, bisoprolol)	I C

What this changes in this draft: under 2026 ESC, the post-MI LVEF 41–49% group moves from “Class IIa” (Q1) to a Class I recommendation — as HFrEF if symptomatic, or as stage B (I B1) if not.

B. Mineralocorticoid receptor antagonists (MRA) in recent AMI with heart failure

An MRA (eplerenone first-line) is indicated after AMI only when LVEF is $\leq 40\%$ with HF or diabetes; routine MRA in unselected MI is not supported (ALBATROSS, CLEAR SYNERGY).

Question 1: What are the primary indications for initiating an MRA after a recent AMI?

Answer: In patients with a recent AMI, an MRA is indicated to reduce cardiovascular mortality and HF hospitalisations in patients who have left ventricular systolic dysfunction (LVEF $\leq 40\%$) and either symptoms of heart failure or concomitant diabetes mellitus, provided there is no severe renal impairment or hyperkalaemia.

Evidence & key guidelines:

- **ACC/AHA/HFSA HF guidelines:** Class I, Level of Evidence A recommendation for post-AMI patients with LVEF $\leq 40\%$ and HF symptoms or diabetes.
- **ESC HF & ACS guidelines:** Class I, Level of Evidence A recommendation for eplerenone in post-MI patients meeting EPHESUS criteria.

Trial summary: EPHEUS

- **P:** 6,632 patients enrolled 3–14 days post-AMI with LVEF $\leq 40\%$ and either clinical HF signs/symptoms or diabetes.

- **I:** Eplerenone 25 mg/day, titrated to 50 mg/day at 4 weeks.
- **C:** Placebo, on top of standard therapy (ACEi/ARB, beta-blockers, aspirin, statins, revascularisation).
- **O:** All-cause mortality reduced (RRR 15%, $p=0.008$); CV mortality or CV hospitalisation reduced (RRR 13%, $p=0.002$); sudden cardiac death reduced 21% ($p=0.03$).

Question 2: What is the optimal starting time for MRA therapy after AMI, and when does benefit begin?

Answer: MRA therapy should be initiated early after AMI, typically between 3 and 14 days post-event (ideally within 7 days if the patient is haemodynamically stable with acceptable renal function and potassium). In trials, significant benefit appears as early as 30 days post-randomisation (sudden cardiac death) and around 3–6 months for all-cause mortality.

Post-hoc analyses of EPHESUS showed that patients who received eplerenone early (<7 days post-AMI) had greater and earlier mortality reductions than those who started at 7–14 days.

Trial summary: EPHESUS early-initiation analysis

- **P:** Post-AMI patients with LVEF $\leq 40\%$, divided by time to randomisation (<7 vs ≥ 7 days).
- **I:** Early eplerenone (<7 days post-MI; median 3 days).
- **C:** Late eplerenone (≥ 7 days) or placebo.
- **O:** Initiation <7 days gave a 31% reduction in all-cause mortality at 30 days ($p=0.004$) versus placebo; benefit on mortality by day 30.

Question 3: How should MRA dosing be adjusted, titrated and monitored post-AMI?

Answer:

- **Starting dose:** Eplerenone 25 mg once daily (or spironolactone 12.5–25 mg once daily).
- **Target dose:** Eplerenone 50 mg once daily (or spironolactone 25–50 mg once daily) at 4 weeks.
- **Prerequisites:** $K^+ < 5.0$ mEq/L and creatinine ≤ 2.5 mg/dL (men) / ≤ 2.0 mg/dL (women), or eGFR > 30 mL/min/1.73 m².

Serum K^+	eGFR / creatinine	MRA dose adjustment (source)
< 5.0 mEq/L	eGFR ≥ 50	Maintain or titrate to 50 mg/day at 4 weeks
5.0–5.4 mEq/L	eGFR 30–49	Halve the dose (e.g., 25 mg alternate days or 12.5 mg daily)
≥ 5.5 mEq/L	eGFR < 30	Withhold until $K^+ < 5.0$, then restart at lower dose

Monitoring: K^+ and renal function at 1 week, 1 month and 3 months, then every 3–6 months.

Serum K^+ (mEq/L)	Action
< 5.0	Continue; up-titrate 25 $\rightarrow$ 50 mg at 4 weeks
5.0–5.4	Keep the current dose
5.5–5.9	Halve the dose (50 $\rightarrow$ 25 mg, or 25 mg $\rightarrow$ alternate days)
≥ 6.0	Stop; restart at 25 mg alternate days once $K^+ < 5.0$

Question 4: What is the evidence for MRA choice in post-AMI HFrEF versus preserved LVEF?

Answer:

- **HFrEF (LVEF ≤40%):** Eplerenone is the drug of choice with Class I evidence in the post-AMI setting (EPHESUS). Spironolactone is supported by broader HFrEF trials (RALES), though RALES enrolled chronic, non-acute HF.
- **Preserved LVEF (≥50%):** In acute MI without low LVEF or HF, routine MRA is not indicated unless treating resistant hypertension. In chronic HFpEF, spironolactone carries a weak recommendation (Class IIb) to reduce hospitalisations; post-MI HFpEF data are mixed or neutral.

Trial summary: ALBATROSS

- **P:** 1,603 patients with acute MI (STEMI and NSTEMI) regardless of LVEF or HF.
- **I:** Early MRA (IV potassium canrenoate, then oral spironolactone 200 mg initial loading, then 25 mg/day for 6 months).
- **C:** Standard therapy alone.
- **O:** No difference in death, resuscitated arrest, ventricular arrhythmia or HF at 6 months (HR 0.97, p=0.81). STEMI subgroup showed lower mortality (exploratory).
- In ALBATROSS the 200 mg loading dose was **IV potassium canrenoate**, followed by oral spironolactone 25 mg daily — there was no 200 mg oral spironolactone load [19]. Other figures are correct.
- RALES: 1,663 patients with severe chronic HFrEF; all-cause mortality RR 0.70 [18]. The chronic HFpEF IIb recommendation (TOPCAT) is from ACC/AHA [4,24].
- **Missing: CLEAR SYNERGY (OASIS-9, 2024–25).** 7,062 patients after PCI for STEMI or large MI, spironolactone 25 mg vs placebo: no reduction in CV death or new/worsening HF, nor in CV death, MI, stroke or HF [21]. Together with ALBATROSS, this closes the door on routine MRA in unselected MI.

Question 5: Spironolactone vs eplerenone vs finerenone — selectivity, side effects, onset

Parameter	Spironolactone	Eplerenone	Finerenone
Selectivity	Non-selective (progesterone/androgen receptors)	Selective	Non-steroidal, highly selective
Gynaecomastia / mastodynia	High (~10%)	Very low (<1%)	Negligible
Key trials	ALBATROSS (unselected MI), RALES (chronic HFrEF)	EPHESUS (post-MI HFrEF)	FIGARO-DKD / FINEARTS-HF
Mean/median onset of benefit	~2–3 months (RALES)	~30 days (EPHESUS)	~1–3 months (CKD/HF trials)
Half-life	13.8–16.5 h (active metabolites)	4–6 h	2–3 h
Primary role post-AMI	Alternative if eplerenone unavailable/costly	First-line post-AMI with LVEF ≤40% + HF/diabetes	Emerging; not standard post-AMI

Question 6: MRA use in post-AMI cardiogenic shock or severe renal impairment

Answer: MRAs are contraindicated in the hyper-acute setting of cardiogenic shock or severe AKI (eGFR <30 mL/min/1.73 m² or K⁺ >5.0 mEq/L). Start only once haemodynamics stabilise, congestion is controlled, and renal function is stable.

Trial summary: REMINDER

- **P:** 1,012 post-STEMI patients without HF and with LVEF >40%, haemodynamically stable.
- **I:** Eplerenone 25–50 mg daily started within 24 hours of symptom onset.
- **C:** Placebo.

- **O:** Reduced the composite (CV death, re-infarction, HF hospitalisation, or raised BNP/NT-proBNP), driven mostly by biomarkers ($p < 0.0001$). Hyperkalaemia higher with eplerenone (4.6% vs 1.2%, $p = 0.001$).

Summary verdict (source): Early initiation requires stable perfusion, no acute renal failure, and close potassium monitoring.

Take-home message — MRA: Give eplerenone 25 mg ($\rightarrow$ 50 mg at 4 weeks) to post-AMI patients with LVEF $\leq 40\%$ plus HF or diabetes, once stable and ideally within 7 days; mortality benefit is visible by 30 days. Check K⁺ and creatinine within the first week. Do not start if K⁺ ≥ 5.0 or eGFR < 30 , and do not give MRAs routinely to all MI patients.

2026 ESC update — MRA [36]

Setting	2026 status	Class / level
Symptomatic HF, any LVEF	FMT — steroidal MRA for HFrEF; steroidal or non-steroidal (finerenone) for HFpEF	I A (revised; was I A for HFrEF only, IIb C for HFmrEF)
Post-MI, LVEF $\leq 40\%$, signs of HF or diabetes	Eplerenone to reduce HF hospitalisation and death	I B1 (new)
T2DM with CKD (stage A prevention)	Finerenone to reduce risk of HF	I A
Pregnancy	Not recommended	III C

What this changes in this draft: MRA is now FMT in both phenotypes, so a post-MI patient with symptomatic HF and LVEF $\geq 50\%$ (HFpEF) also qualifies. **Routine MRA in MI without HF is still unsupported** (ALBATROSS, CLEAR SYNERGY) [19,21]. Potassium and eGFR rules in Q3 are unchanged.

C. ARNI / ARB in recent AMI with heart failure

An ACE inhibitor within 24 hours remains first-line after AMI with HF or LVEF $\leq 40\%$; valsartan replaces it if not tolerated, and sacubitril/valsartan is for established HFrEF, not routine post-MI prevention (PARADISE-MI neutral).

Question 1: What are the primary indications for an ARNI or ARB after a recent AMI?

Answer:

- **ARBs:** Indicated in post-AMI patients with HF, LV systolic dysfunction (typically LVEF $\leq 40\%$), or signs of HF who are intolerant to ACE inhibitors; also for hypertension or diabetic kidney disease post-AMI.
- **ARNI (sacubitril/valsartan):** Indicated for established chronic HFrEF post-AMI once stable. **It is not FDA-approved or guideline-recommended for acute post-AMI prevention** without established HF/LVSD, nor for primary prevention in post-AMI preserved EF.

Question 2: What is the optimal starting time for ARNI or ARB after AMI?

Answer:

- **ARBs:** Initiate early, within **24–48** hours, if haemodynamically stable (SBP > 100 mmHg, no worsening renal failure, no hyperkalaemia).
- **ARNI — de novo post-AMI:** Trials started a median of 4.3 days (range 0.5–7 days) after PCI or symptom onset.

- **ARNI — acute decompensated HF post-AMI:** Start in stable inpatients after 24 hours of haemodynamic stability (no IV inotropes or IV diuretic escalation for 24 hours). A 36-hour washout is required when switching from an ACE inhibitor.

Question 3: How should ARNI and ARB doses be started and adjusted?

Answer:

- **ARB (valsartan):** Start 20 mg BID (or 40 mg BID); double every few days to weeks toward 160 mg BID (VALIANT protocol).
- **ARNI (sacubitril/valsartan):** Start 24/26 mg BID if ACEi/ARB-naïve, on low-dose ACEi/ARB, or eGFR <30 mL/min/1.73 m²; start 49/51 mg BID if on standard-to-high dose ACEi/ARB. Double every 2–4 weeks to 97/103 mg BID. Halve or hold if SBP <95 mmHg, K⁺ >5.5 mEq/L, or creatinine rises >50%.

Question 4: ARNI vs ARB in post-AMI reduced vs preserved EF

Answer:

- **LVEF ≤40%:** If chronic HFrEF existed before or persists after AMI, ARNI is preferred over ACEi/ARB (PARADIGM-HF). In the acute post-AMI setting, ARNI is not superior to ACE inhibitors (PARADISE-MI); an ACE inhibitor (or ARB if intolerant) remains standard first-line.
- **LVEF 41–49% or ≥50%:** ARNI may be considered in mildly reduced or lower-range preserved EF (especially women and LVEF <57–60%, PARAGON-HF subgroups). ARBs are indicated for coexisting hypertension, diabetes or renal disease but do not reduce CV mortality in pure HFpEF.

Question 5: When does clinical benefit begin in the major ARNI/ARB trials?

Answer:

- **VALIANT (valsartan post-AMI):** Benefit detectable within the first 30 days (mortality curves separating within 14–30 days).
- **PARADISE-MI:** Median follow-up 16 months; separation of exploratory outcomes (total HF events) at about 1–3 months; primary endpoint not significant.
- **PIONEER-HF:** NT-proBNP reduction significant as early as week 1.
- **PARADIGM-HF:** Primary outcome curves separated within 30 days.
- **PARAGON-HF:** Benefit in responders (LVEF ≤57%) around 3–6 months.

Question 6: PICO summaries of landmark ARNI and ARB trials

1. VALIANT (post-AMI LVSD/HF — ARB vs ACEi)

- **P:** 14,703 patients 0.5–10 days (mean 4.9) after AMI with LVSD (LVEF ≤40%) or clinical HF.
- **I:** Valsartan titrated to 160 mg BID.
- **C:** Captopril 50 mg TID, or valsartan + captopril.
- **O:** All-cause mortality 19.9% vs 19.5% (HR 1.00, p=0.98). Onset of benefit: divergence within 14–30 days. Conclusion: valsartan non-inferior to captopril.

2. PARADISE-MI (post-AMI high risk — ARNI vs ACEi)

- **P:** 5,661 post-AMI patients (median 4.3 days) with LVEF ≤40% and/or pulmonary congestion, plus at least one risk enhancer.
- **I:** Sacubitril/valsartan titrated to 97/103 mg BID.
- **C:** Ramipril titrated to 5 mg BID.

- **O:** CV death, first HF hospitalisation or outpatient HF: 338 events (11.9%) vs 373 (13.2%); HR 0.90, p=0.17. Trend toward benefit at 30–90 days. Conclusion: not superior to ramipril.

3. PIONEER-HF (acute decompensated HF in hospital — ARNI)

- **P:** 881 patients hospitalised with acute decompensated HFrEF (LVEF ≤40%), stabilised.
- **I:** Sacubitril/valsartan titrated to 97/103 mg BID.
- **C:** Enalapril 10 mg BID.
- **O:** Time-averaged NT-proBNP reduction at weeks 4 and 8: −46.7% vs −25.3% (p<0.001); significant at week 1. In-hospital ARNI start is safe.

4. PARADIGM-HF (chronic HFrEF — ARNI vs ACEi)

- **P:** 8,442 patients with chronic HFrEF (LVEF ≤40%, later ≤35%).
- **I:** Sacubitril/valsartan 97/103 mg BID.
- **C:** Enalapril 10 mg BID.
- **O:** CV death or HF hospitalisation 21.8% vs 26.5% (HR 0.80, p<0.001); separation within 30 days.

5. PARAGON-HF (HFpEF — ARNI vs ARB)

- **P:** 4,796 patients with HF and LVEF ≥45%.
- **I:** Sacubitril/valsartan 97/103 mg BID.
- **C:** Valsartan 160 mg BID.
- **O:** Total HF hospitalisations and CV death: rate ratio 0.87, p=0.06. Benefit in LVEF ≤57% and women.

Take-home message — ARNI/ARB: After AMI with HF or LVEF ≤40%, start an ACE inhibitor within 24 hours once SBP is above 100 mmHg; use valsartan (20 → 160 mg BID) if ACEi-intolerant. Reserve sacubitril/valsartan for established or persisting HFrEF, switching only after a 36-hour ACEi washout. PARADISE-MI did not show ARNI beats ramipril early after MI.

2026 ESC update — ACE-I / ARNI / ARB [36]

Setting	2026 status	Class / level
Symptomatic HFrEF (now LVEF <50%)	FMT — ACE-I or ARNI	Class I
HFrEF intolerant of ACE-I or ARNI	ARB	Class I (as FMT alternative)
Stage B, LVEF ≤40% (includes post-MI LV dysfunction)	ACE-I, or ARB if ACE-I not tolerated	I A (new)
Symptomatic HFpEF	ACE-I/ARB/ARNI may be considered to reduce HF hospitalisation — AMT	IIb C (new)
Pregnancy	Not recommended	III C

D. SGLT2 inhibitors in recent AMI with heart failure

SGLT2 inhibitors are indicated after AMI when heart failure is established (any LVEF), or for diabetes or CKD; routine use in every MI is not proven, because both dedicated post-MI trials missed their hard primary endpoints.

Question 1: What are the primary indications for an SGLT2 inhibitor after a recent AMI?

Answer: After a recent AMI, SGLT2 inhibitors (dapagliflozin or empagliflozin) are indicated to reduce HF hospitalisations and urgent HF visits in patients with LV systolic dysfunction (LVEF $\leq 45\%$ or $\leq 50\%$) and/or clinical signs or symptoms of congestion during the index admission, regardless of type 2 diabetes.

Contemporary trials (EMPACT-MI and DAPA-MI) show that routine post-AMI SGLT2i mainly prevents HF admissions and cardiometabolic decompensation rather than re-infarction. SGLT2i therapy is recommended across the LVEF spectrum (HFrEF, HFmrEF, HFpEF) once stable.

Clear indications are: (1) established HF of any LVEF — Class I in ESC 2023 focused update and ACC/AHA 2022 for HFrEF [4,34]; (2) type 2 diabetes; (3) CKD. For congestion or LVEF $< 45\%$ after MI, EMPACT-MI supports use to lower first HF hospitalisation, as a reasonable but not guideline-mandated choice [30].

Question 2: When should SGLT2i be started post-AMI, and when does benefit begin?

Answer: Start in hospital before discharge, typically within **1–14 days** post-AMI (trial median 5–8 days), once stable, off IV inotropes and out of shock.

- **EMPACT-MI (empagliflozin):** median 5 days post-AMI (enrolled within 14 days).
- **DAPA-MI (dapagliflozin):** median 8 days post-AMI (enrolled within 10 days).
- **Onset of benefit:** HF hospitalisation curves separate within 14–30 days.

Question 3: Dosing, titration and adjustment

Answer: SGLT2 inhibitors do not need step-wise titration.

SGLT2 inhibitor	Fixed daily dose	eGFR threshold to start	Dose adjustment
Dapagliflozin	10 mg once daily	≥ 25 mL/min/1.73 m ²	Single fixed dose; no adjustment for mild–moderate renal or hepatic impairment
Empagliflozin	10 mg once daily	≥ 20 mL/min/1.73 m ²	Single fixed dose; no adjustment down to eGFR cutoff

- **Initial eGFR dip:** A transient 10–15% fall is haemodynamic (tubuloglomerular feedback) and should not prompt discontinuation unless eGFR falls $> 30\%$ without stabilising.
- **Diuretic adjustment:** If on high-dose loop diuretics and euvoaemic, consider cutting the loop diuretic by 20–25% to prevent hypovolaemia/orthostasis.

Question 4: How does LVEF influence choice and efficacy of SGLT2i post-AMI?

Answer: SGLT2 inhibitors show consistent benefit across all LVEF categories.

- **Post-AMI HFrEF (LVEF $\leq 40\%$):** One of the four GDMT pillars; reduce CV death/HF hospitalisation and slow renal decline (extrapolated from DAPA-HF and EMPEROR-Reduced).

Consistent benefit across LVEF is proven in *chronic heart failure* (DAPA-HF, EMPEROR-Reduced, and HFmrEF/HFpEF trials) [32–34]. EMPACT-MI enrolled LVEF $< 45\%$ or congestion, and DAPA-MI enrolled impaired LV function or Q-wave MI — neither was an HFmrEF/HFpEF trial [30,31].

Question 5: Safety, contraindications and sick-day rules

Answer:

- **Contraindications:** Type 1 diabetes, active DKA, severe AKI (eGFR below threshold), dialysis.
- **Euglycaemic DKA:** Can occur with near-normal glucose (<250 mg/dL); patients should report nausea, vomiting, abdominal pain or dyspnoea.
- **Genital mycotic infections:** Higher risk; advise hygiene.
- **Sick-day protocol:** Withhold during acute severe illness, major surgery, prolonged fasting, or volume depletion/sepsis.

Question 6: Trial evidence in acute post-AMI populations (PICO)

1. EMPACT-MI (empagliflozin post-AMI)

- **P:** 6,522 patients hospitalised with acute MI (median 5 days) with LVEF <45% or congestion during admission.
- **I:** Empagliflozin 10 mg once daily plus standard care.
- **C:** Placebo.
- **O:** all-cause death no difference. First HF hospitalisation: 23% relative reduction (HR 0.77, 95% CI 0.60–0.98). Curves separated within 14–30 days.

Answer check: ❌ **p-value wrong.** Published primary result: HR 0.90 (95% CI 0.76–1.06), **p=0.21** [30]. First HF hospitalisation HR 0.77 (0.60–0.98) is correct but was a secondary, not formally tested, outcome. All-cause death alone: no difference.

2. DAPA-MI (dapagliflozin post-AMI without prior diabetes/HF)

- **P:** 4,017 patients with acute MI and impaired LV function (LVEF <50%) or Q-wave MI, without prior diabetes or chronic HF.
- **I:** Dapagliflozin 10 mg once daily (median 8 days post-AMI).
- **C:** Placebo.
- **O:** Hierarchical win ratio 1.34 (p<0.001), driven by cardiometabolic outcomes (weight, T2DM prevention, glycaemia). Consistent reduction in composite HF events. Metabolic separation at 1 month.

Summary matrix: post-AMI SGLT2i (source, corrected in brackets)

Parameter	Dapagliflozin	Empagliflozin
Post-AMI trial	DAPA-MI	EMPACT-MI
Median time to start	8 days [verify]	5 days
Dose	10 mg once daily (fixed)	10 mg once daily (fixed)
eGFR threshold	≥25 mL/min/1.73 m ²	≥20 mL/min/1.73 m ²
Onset of benefit	[Cardiometabolic only; no HF/death benefit]	14–30 days (first HF hospitalisation, secondary)
Main clinical impact	Weight loss, less new T2DM	[Primary endpoint neutral]; 23% fewer first HF hospitalisations

Take-home message — SGLT2 inhibitors: After AMI, start dapagliflozin or empagliflozin 10 mg once daily (no titration) before discharge in anyone with established HF at any LVEF, type 2 diabetes or CKD, once stable and eGFR ≥20–25. In LV dysfunction or congestion without an HF diagnosis, benefit is limited to fewer HF admissions. Watch for euglycaemic DKA and hold on sick days.

2026 ESC update — SGLT2 inhibitors [36]

Setting	2026 status	Class / level
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Setting	2026 status	Class / level
Symptomatic HF, any LVEF	FMT in both HFrEF and HFpEF	Class I
Decompensated HF, after initial stabilisation	In-hospital initiation to improve QoL and congestion and reduce HF hospitalisation	I B1 (new)
T2DM with ASCVD or multiple risk factors (stage A)	Prevent HF and CV death	I A
T2DM with CKD (stage A)	Prevent HF or CV death	I A
Pregnancy	Not recommended	III C

E. Four-pillar GDMT timeline and sequencing algorithm

The source's sequence is sound in outline; it needs the indication limits from Sections A–D applied to each step. Starting all indicated drugs before discharge and titrating fast is supported by STRONG-HF in acute HF [35], though that trial was not post-MI-specific.

Corrected sequence at a glance — all four pillars can start before discharge once the patient is stable. Delay any step if SBP is under 100 mmHg, K⁺ is 5.0 mEq/L or more, or the patient is in shock.

Phase	Action
Day 0 · Admission	Reperfuse and stabilise. No IV beta-blocker if HF. Hold oral HF drugs while in shock.
Day 1 (within 24 h)	Oral beta-blocker; ACE inhibitor, or ARB — if SBP ≥100 mmHg, no shock, HR ≥60 bpm, Killip I–II.
Days 2–3	Eplerenone 25 mg if LVEF ≤40% + HF or diabetes, K ⁺ <5.0, eGFR ≥30. First up-titration.
Discharge (days 3–7)	SGLT2i 10 mg if HF, T2DM or CKD. ARNI only for HFrEF, after 36-hour ACEi washout.
Week 1–2 visit	K ⁺ and creatinine; expect a small eGFR dip. Double beta-blocker and ACEi/ARNI if SBP ≥100, HR ≥60.
Week 4 visit	Repeat K ⁺ ; adjust MRA by potassium rules. Eplerenone 25 → 50 mg; keep titrating to target.

Step 1: Pre-initiation safety and haemodynamic screening (first 12–24 h after reperfusion)

- **Haemodynamics:** SBP ≥100 mmHg; HR ≥60 bpm; Killip I–II (no pulmonary oedema or shock).
- **Renal:** eGFR ≥30 mL/min/1.73 m²; no acute oliguria/AKI (creatinine doubling).
- **Electrolytes:** K⁺ <5.0 mEq/L; no severe acidosis.

Step 2: Phase-wise in-hospital sequencing

Phase 1 — Day 1 (first 24 h after reperfusion)

- **Oral beta-blocker:** metoprolol succinate 12.5–25 mg daily, bisoprolol 1.25–2.5 mg daily, or carvedilol 3.125 mg BID. Criteria: HR ≥60 bpm, SBP ≥100 mmHg, Killip I/II, no IV inotropes.
- **ACE inhibitor (ARB if intolerant):** ramipril 1.25–2.5 mg BID, lisinopril 2.5–5 mg daily, or valsartan 20–40 mg BID. Criteria: SBP ≥100 mmHg, stable creatinine, K⁺ <5.0 mEq/L.

Phase 2 — Days 2–3

- **MRA:** eplerenone 25 mg daily (or spironolactone 12.5–25 mg daily) if LVEF ≤40% **and** HF symptoms or diabetes; K⁺ <5.0 mEq/L, eGFR ≥30.
- **First titration:** if SBP >110 mmHg and HR ≥65 bpm, step up beta-blocker and ACEi/ARB.

Phase 3 — Day 4 / discharge (days 3–7)

- **SGLT2i:** empagliflozin or dapagliflozin 10 mg daily for LVEF $\leq 45\text{--}50\%$ or congestion during admission; eGFR $\geq 20\text{--}25$; no titration.
- **ARNI transition:** in de novo post-AMI, continue ACEi/ARB (PARADISE-MI). If chronic HFrEF existed or severe post-MI HF develops, switch to ARNI after a strict 36-hour ACEi washout.

Step 3: Patient-specific sequencing matrix

Clinical scenario	First line (Day 1)	Second line (Days 2–3)	Third line (pre-discharge)	Special considerations (source)	Answer check
STEMI/NSTEMI with HFrEF (LVEF $\leq 40\%$)	Oral beta-blocker + ACEi (or ARB)	MRA (eplerenone 25 mg)	SGLT2i 10 mg	All 4 pillars required before discharge	✓ Correct as a goal; “aim for” rather than “required” — start what is safe and titrate after discharge [35]
Post-AMI with preserved EF (LVEF $\geq 50\%$)	Oral beta-blocker + ACEi/ARB	Hold MRA (unless T2DM/resistant HTN)	SGLT2i 10 mg	Beta-blocker per REDUCE-AMI/REBOOT	✗ Those trials show no benefit of beta-blockers at LVEF $\geq 50\%$ without another indication [10,11,14]. SGLT2i only if HF, T2DM or CKD. MRA not indicated (CLEAR SYNERGY) [21]
Borderline SBP (90–100 mmHg)	Low-dose SGLT2i + low-dose beta-blocker	Low-dose MRA	Low-dose ACEi/ARB	SGLT2i and MRA lower BP less than ACEi/ARNI	☐ Sound logic, but SGLT2i has no low dose — 10 mg is the only dose
Impaired renal function (eGFR 25–45)	Beta-blocker + SGLT2i	Low-dose ACEi/ARB	Half-dose MRA (12.5 mg)	SGLT2i protects kidneys despite a 10–15% eGFR dip	☐ MRA contraindicated if eGFR < 30 ; at 30–49 use eplerenone 25 mg alternate days [3]. Dapagliflozin needs eGFR ≥ 25

Step 4: Early outpatient follow-up

- **Week 1–2 visit:** check K⁺ and creatinine/eGFR; accept an initial eGFR fall up to 15–20%. Double beta-blocker and ACEi/ARB if SBP ≥ 100 mmHg and HR ≥ 60 bpm.
- **Week 4 visit:** repeat K⁺ (adjust MRA if K⁺ ≥ 5.5 mEq/L). Advance MRA from 25 to 50 mg daily; keep titrating beta-blocker and ACEi/ARNI toward trial target doses.

Take-home message — Sequencing: Screen first (SBP, HR, Killip class, K⁺, eGFR). Day 1: oral beta-blocker and ACEi. Days 2–3: eplerenone if LVEF $\leq 40\%$ with HF or diabetes. Before discharge: SGLT2i when HF, T2DM or CKD is present. Then titrate every 1–2 weeks with labs — in shock or K⁺ ≥ 5.0 , wait.

2026 update: new heart failure classification and management strategy

The 2026 ESC Heart Failure Guidelines (published 28 August 2026) redefine HFrEF as LVEF $< 50\%$, drop HFmrEF, and regroup treatment into foundational medical therapy (FMT), additional medical therapy (AMT) and guideline-directed interventional therapy (GDIT) [36]. The Second Universal Definition of Heart

Failure (AHA/ACC/ESC/WHF, 2026) keeps stages A–D and groups HF as reduced, preserved or improved EF, with a new classification by cause [37].

What changed

Item	2021/2023 ESC	2026 ESC [36]
LVEF phenotypes	HFrEF ≤40%, HFmrEF 41–49%, HFpEF ≥50%	HFrEF <50%; HFpEF ≥50% with objective evidence of diastolic dysfunction/raised filling pressures, supported by natriuretic peptides
Improved EF	Not a separate management category	LVEF rise ≥10 points (absolute) and above 40%; keep FMT at highest tolerated dose (I C)
Stages	Not used by ESC	A at risk · B pre-HF (structural disease or LV dysfunction, no symptoms) · C symptomatic HF · D advanced HF
Acute HF	“Acute heart failure”	Decompensated HF (DHF) , managed in 3 phases: initial management → stabilisation → pre-discharge/early post-discharge
Treatment terms	GDMT	GDMT = FMT + AMT ; devices and procedures = GDIT
Evidence grading	Levels A, B, C	New ESC grading (considers studytype, number, power, bias); levels now include B1 and B2

New treatment nomenclature

Category	Definition	HFrEF (LVEF <50%)	HFpEF (LVEF ≥50%)
FMT — foundational medical therapy	Class I for the general HF population, with proven morbidity/mortality benefit	Beta-blocker · ACE-I/ARNI/ARB · MRA · SGLT2i	MRA · SGLT2i
AMT — additional medical therapy	Class IIa/IIb, or Class I only for symptoms/QoL or for specific subsets	Loop diuretics, potassium binders, ivabradine, vericiguat, hydralazine–ISDN, cardiac glycosides, cardiac myosin activator	Loop diuretics; ACE-I/ARB/ARNI (IIb C); semaglutide or tirzepatide if BMI ≥30 and LVEF ≥45% (IIa B1)
GDIT — guideline-directed interventional therapy	Any device or procedure with a guideline recommendation	ICD, CRT, conduction-system pacing, mitral TEER, temporary/durable MCS, transplant	Device and procedural options per comorbidity

“Optimal FMT” means FMT at the highest tolerated guideline target doses [36].

How the new classification applies to recent AMI

Post-MI situation	2026 label	Strategy [36]
MI, normal LV, no HF	Stage A (at risk)	Risk-factor control; routine beta-blocker not supported when LVEF >50% (REDUCE-AMI; pooled trials)
MI, LVEF <50%, no HF symptoms	Stage B (pre-HF)	Beta-blocker (I B1); ACE-I, or ARB if intolerant, if LVEF ≤40% (I A); eplerenone if LVEF ≤40% with HF signs or diabetes (I B1)
MI with HF and LVEF <50% (includes old HFmrEF 41–49%)	Stage C, HFrEF	All four FMT classes; up-titrate every 1–2 weeks (I C)
MI with HF and LVEF ≥50%	Stage C, HFpEF	FMT = MRA + SGLT2i
MI with decompensation	DHF	Stabilise, then start SGLT2i in hospital (I B1); phase-based management
AMI cardiogenic shock	DHF / shock	Microaxial flow pump considered in STEMI shock with LV dysfunction and no hypoxic brain injury (IIa B1); no temporary MCS in unselected AMI shock (III B1); no IABP in unselected shock (III B1)

Two classifications to keep apart: ESC 2026 uses two phenotypes (<50% / ≥50%). The 2022 AHA/ACC/HFSA guideline, still current in the US, keeps HFmrEF [4]. Check which one your institution's protocols follow.

Uptitration and continuation (new Class I C): Up-titrate FMT at least every 1–2 weeks to trial target doses, guided by symptoms, vital signs and labs. Continue FMT at the highest tolerated dose even if the patient becomes asymptomatic or LVEF improves [36].

G. Overall take-home messages for the emergency physician and intensivist

1. **Stabilise first, then start drugs.** No oral HF drug in shock, pulmonary oedema, SBP <100 mmHg or rising lactate. No IV beta-blocker in any patient with HF signs (COMMIT) [5].
2. **LVEF ≤40% after AMI = full treatment.** Oral beta-blocker and ACE inhibitor within 24 hours, eplerenone once K⁺ <5.0 and eGFR ≥30 (if HF or diabetes), and SGLT2i before discharge when HF is established [1–4,15].
3. **LVEF 40–49%:** beta-blockers now have pooled RCT support (HR 0.75) [13]; ACE inhibitor as standard [1,2].
4. **LVEF ≥50%, no HF, no other indication:** beta-blockers and MRAs give no proven benefit (REDUCE-AMI, REBOOT, pooled 17,801 patients; CLEAR SYNERGY) [10,11,14,21].
5. **ARNI is not a post-MI drug; it is an HFrEF drug.** PARADISE-MI was neutral versus ramipril [26]. Switch only for established HFrEF, after 36 hours off ACEi.
6. **SGLT2i after MI:** clear benefit when HF, diabetes or CKD is present; in MI alone, EMPACT-MI and DAPA-MI missed their hard endpoints [30,31].
7. **Safety labs drive titration.** K⁺ and creatinine within the first week after MRA or RAS inhibitor; halve eplerenone at K⁺ 5.5–5.9, stop at ≥6.0 [3,15]. Check ketones in any acidotic patient on SGLT2i.
8. **Never stop a beta-blocker abruptly** in a stable patient; reduce or hold only for bradycardia, block, shock or severe decompensation.
9. **Use the 2026 labels.** Under ESC 2026, post-MI HF with LVEF <50% is HFrEF and gets all four FMT classes; HF with LVEF ≥50% is HFpEF and gets MRA + SGLT2i. Up-titrate every 1–2 weeks and do not stop FMT when LVEF improves [36].