



REVIEW

# Clinical Decision Pathway for the Use of Fondaparinux in the Management of Acute Coronary Syndrome (ACS) in Hospitals with and Without Catheter Laboratories: An Expert Opinion from India

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## ABSTRACT

The current recommendations by Indian experts who are focused on the challenges in the management of patients with acute coronary syndrome (ACS) in rural areas, due to limited catheterization (CATH) lab facilities and interventional cardiologist coverage across the country, are described. 120 cardiologist experts drafted recommendations during ten advisory board meetings conducted from April to May 2022. Experts framed statements based on experience, collective clinical judgment from practical experience, and available scientific evidence regarding ACS. The consensus

positioned fondaparinux as highly useful in non-CATH-lab-based hospitals for patients diagnosed with non-ST elevation acute coronary syndrome (NSTEMI-ACS) and ST elevation acute coronary syndrome (STEMI-ACS) patients who cannot be shifted to percutaneous coronary intervention (PCI)-capable centres, or for patients who are thrombolysed at peripheral centres.

**Keywords:** Acute coronary syndrome; Anticoagulant; Fondaparinux; Percutaneous coronary intervention

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### Key Summary Points

ACS accounts for 3 million fatalities (25% of all deaths) annually in India, and the availability and accessibility of PCI-equipped centres and qualified technicians is limited in rural parts of India.

120 cardiologists drafted seven consensus statements based on the available literature, clinical experience, and their expert opinion.

Fondaparinux is used if the patient denies PCI, if PCI facilities are unavailable, or if PCI is contraindicated (due to old age or comorbid conditions).

In non-CATH lab-based hospitals, fondaparinux is useful in NSTEMI-ACS and STEMI-ACS patients who cannot be shifted to PCI-capable centres, and for patients who are thrombolysed at peripheral centres or receive no other form of reperfusion therapy.

Fondaparinux is also recommended in CATH lab-based hospitals if the patient is diagnosed with NSTEMI-ACS or STEMI-ACS and PCI cannot be performed or PCI is delayed.

## INTRODUCTION

### Current Scenario

Acute coronary syndrome (ACS) is one of the foremost causes of mortality worldwide. India has a tremendous ACS load globally, with a burden 3–4 times that of America, 6 times that of China, and 20 times that of Japan. ACS accounts for 3 million fatalities (25% of all deaths) annually in India [1, 2]. One of the main challenges in rural communities is the combination of health disparities not necessarily found in larger communities and limited

services for managing critical conditions like ACS. Thus, cardiologists in a rural setting face a medically underserved population, which results in a patient base that traditionally has little or no preventive care, which equates to higher mortality rates.

In 1960, urban India had a 2% prevalence of ischemic heart disease, but by 2013, this had increased by approximately 7 times to 14%. Similarly, rural areas experienced an increase in prevalence, with the disease more than quadrupling from 1.7 to 7.4% between 1970 and 2013. Among individuals living in villages, the prevalence of coronary heart disease was 1.7% for males and 1.5% for females [3]. A significant ACS registry from Kerala also found that over 40% of patients with ST-segment elevation MI sought medical attention more than 6 h after experiencing symptoms. Furthermore, the quality of medical care received in rural areas during and after hospitalization was inferior compared to that provided in urban areas [4].

Another priority for rural populations should be timely connectivity to hospitals with well-equipped centres for ACS patients. The lack of primary care leads to emergency departments being overburdened with non-urgent medical needs. This is necessary when transporting patients, such as those experiencing an ST elevation ACS (STEMI-ACS), from areas more than 30 min away [5].

India has the highest burden of ACS globally, yet little is known about the treatments and outcomes of these diseases [6]. There is an inverse relation between mortality rates and socio-economic strata of patients. Due to a lack of timely intervention, the actual mortality is likely higher than reported, and the difference across socioeconomic strata might be more pronounced [7].

The availability and accessibility of PCI-equipped centres and qualified technicians is limited in rural parts of India. Furthermore, international guidelines for ACS management are not standardized in India and may not be suitable in all geographies. Hence, there is an urgent need for expert recommendations and an adaptable protocol for the management of ACS specifically in rural areas. This document provides adequate guidance for doctors working

in non-catheterization (CATH)-lab-based hospital settings without cardiologist support where a simple guide or treatment protocol could be useful for achieving better initial management of patients arriving with a symptom of ACS. This article does not contain any new studies with human participants or animals performed by any of the authors.





### Diagnosis of ACS (NSTE-ACS and STE-ACS)

ACS refers to any constellation of clinical symptoms similar to acute myocardial ischaemia. ACS is categorized into ST elevation ACS (STE-ACS), non-ST elevation ACS (NSTE-ACS), and unstable angina (UA). STE-ACS occurs due to the complete and prolonged occlusion of an epicardial coronary blood vessel and is defined based on confirmatory tests: ECG criteria and troponin levels (Fig. 1). Globally, 38% of patients who present to a hospital with ACS have an ST-elevation myocardial infarction [8]. NSTE-ACS usually occurs due to severe coronary artery narrowing, transient occlusion, or microembolization of the thrombus or atheromatous material. NSTE-ACS patients have symptoms consistent with ACS and troponin

elevation but no electrocardiogram (ECG) changes consistent with STE-ACS. Unstable angina and NSTE-ACS differ primarily in the presence or absence of a detectable troponin leak [9]. The history, a physical examination, an ECG, biochemical markers, and an echocardiogram (ECHO) are essential for making an appropriate diagnosis [10]. ECG availability and ECG-based diagnosis remains the crucial primary step for diagnosing and managing any case of ACS. If a patient presents with ST elevation or anterior ST depression, it should be considered a STEMI until proven otherwise and treated as such. Transient ST elevation, ST depression, or new T-wave inversions are indicative of NSTEMI. To diagnose NSTEMI, patients must have symptoms consistent with acute coronary syndrome (ACS) and elevated troponin levels but no ECG changes consistent with STEMI. The primary difference between unstable angina and NSTEMI is the presence or absence of a detectable troponin leakage [9].

### Management of ACS

The initial goal of therapy for ACS is focused on stabilizing the patient’s condition, relieving

Chest pain	Onset over minutes	Substernal/midline	Chest pain radiates to epigastric	Radiation down either arm to jaw	Exertional with Pressure and tightness
ECG	 Normal ECG	 ST depression (mild)	 ST depression	 ST elevation	
Increase in Troponin level at 0 hr	No	No	No/Mild	Mild to moderate	Moderate to severe
Troponin change (within 1, 2 or 3 hrs)	No	No	No/Mild	Mild to moderate	Moderate or direct rule in
Diagnosis	↓ Noncardiac	↓ Noncardiac or unstable angina or other cardiac causes	↓ Noncardiac or Unstable Angina	↓ Other cardiac causes or N-STEMI	↓ N-STEMI or STEMI or other cardiac causes

**Fig. 1** Diagnostic tests to differentiate acute coronary syndrome. ECG electrocardiogram, MI myocardial infarction, NSTEMI non-ST elevation myocardial infarction,

STEMI ST elevated myocardial infarction. Adapted from Collet et al. [25]

ischaemic pain, and providing antithrombotic therapy to reduce myocardial damage and prevent further ischaemia. Initial management includes morphine, oxygen, sublingual or intravenous nitro-glycerine, aspirin (162–325 mg), and clopidogrel (300–600 mg loading dose). High-risk patients with NSTEMI-ACS are managed with aspirin, clopidogrel, unfractionated heparin, or low-molecular-weight heparin (LMWH), intravenous platelet glycoprotein IIb/IIIa complex blockers (e.g. tirofiban, eptifibatid), and a beta-blocker for early revascularization [11, 12].

For over a decade, aspirin and clopidogrel have been the standard of care for preventing major thrombotic events in patients undergoing percutaneous coronary intervention (PCI). The PLATO study compared ticagrelor and clopidogrel in patients with either ST-elevation or non-ST-elevation acute coronary syndrome and found that ticagrelor use was associated with a 16% reduction in the first occurrence of vascular death, MI, or stroke compared to clopidogrel [13] (Table 1).

Based on the evidence summarized above and the institute-specific protocols, the physician's discretion, and patient requirements, appropriate antiplatelet therapy to manage ACS can be decided upon.

Anticoagulant therapies form the cornerstone of ACS management. Previously, unfractionated heparin (UFH) was the most commonly used parenteral anticoagulant; however, there are limitations with UFH, such as an adjustable dose–response, a small therapeutic window that requires frequent monitoring, and a higher risk of side effects such as heparin-induced thrombocytopenia, severe haemorrhage, and osteoporosis [6]. Enoxaparin, a LMWH, has primarily replaced unfractionated heparin in clinical practice due to fewer side effects, its higher anti-factor (AFXa) activity, and its more predictable dose–response relationship. However, heparin-induced thrombocytopenia (HIT) still remains the most clinically relevant non-haemorrhagic complication. In contrast to heparin and LMWHs, fondaparinux does not bind to PF4, most likely because it has fewer negatively charged sulfate groups than heparinoids and lacks the sugar domain

required to bind to PF4. More extensive clinical trials in which patients received fondaparinux failed to show any HIT cases [17].

The use of anticoagulants is limited due to several factors. One of these factors is inadequate knowledge and awareness of the efficacy and safety of anticoagulants in managing ACS. Additionally, primary healthcare professionals at nursing homes who do not have CATH labs are hesitant to prescribe anticoagulants because of the risk of bleeding. Poor adherence to medication and routine monitoring is also a barrier to anticoagulation. Patient self-monitoring and self-management are not fully utilized [18]. In the same context, the OASIS-6 trial investigated the effectiveness of fondaparinux in STEMI patients. The study found that fondaparinux was more effective in preventing death or MI at 30 days compared to unfractionated heparin in patients receiving thrombolytic therapy (HR = 0.79;  $P = 0.003$ ) [19] (Table 2).

The introduction of fondaparinux was a fundamental milestone in anticoagulation because it provided proof of the concept of selective factor Xa inhibition with excellent clinical results [24].

According to the 2020 European Society of Cardiology (ESC) guidelines, fondaparinux is recommended as a choice of antithrombotic treatment in NSTEMI-ACS patients without atrial fibrillation who are to undergo PCI intervention following a delay while the patient is transferred within a stipulated time frame. A single bolus of UFH is administered at the time of PCI to prevent the risk of catheter thrombosis [25].

The ESC guidelines (2017) recommend daily fondaparinux after an STEMI-ACS patient has been treated with streptokinase. As per the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, fondaparinux is recommended for index hospitalization for up to 8 days or until revascularization when there is any anticipated delay to performing primary PCI within 120 min [26] (Table 3).

**Table 1** Summary of practice recommendatios

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 Recommendation of fondaparinux in the management of ACS in rural non-CATH-lab-based hospitals

- 1 Fondaparinux 2.5 mg, s.c. once daily should be used for medical management of ACS where PCI is delayed or denied by patients or is unavailable or contraindicated
- 2 Fondaparinux 2.5 mg, s.c. OD highly preferred over enoxaparin in ACS management
- 3 Fondaparinux 2.5 mg IV bolus followed by fondaparinux 2.5 mg s.c. OD after 24 h should be recommended in STE-ACS patients, particularly in those patients who are not undergoing primary PCI, in patients who receive no form of reperfusion therapy, or in patients who receive thrombolytic therapy (streptokinase), as it reduces mortality risk and reinfarction

## Recommendation of fondaparinux in the management of ACS in CATH-lab-based hospitals

- 4 In patients with NSTEMI-ACS that received fondaparinux 2.5 mg OD before undergoing PCI, UFH 50-100 U/kg prior to PCI is recommended to prevent adverse outcomes like catheter-related thrombosis in the CATH lab
- 5 Fondaparinux 2.5 mg s.c. should be recommended for patients with NSTEMI-ACS undergoing early PCI, as it lowers severe bleeding while maintaining the same effectiveness as enoxaparin

## Recommendation regarding bleeding in hospitals and its effect on morbidity and mortality within 1 month of ACS

- 6 A detailed clinical history is essential for patients with comorbid conditions which increase the risk of them having a bleeding event on anticoagulant therapy
  - 7 Fondaparinux 25 mg, s.c. OD can be used in ACS individuals with renal impairment ( $\text{CrCl} > 30 \text{ ml/min}$  and  $\text{eGFR} > 20 \text{ ml/min/1.73 m}^2$ ) and with caution in elderly patients above 60 years of age with no history of severe anemia or renal impairment
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**Table 1** continued

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 Recommendation of fondaparinux for post-procedural anticoagulation

- 8 Fondaparinux is required in the post-PCI setting in cases of angioplasty, multiple stent implantation, atrial fibrillation, a large MI, or large thrombus formation
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## THE NEED FOR EXPERT RECOMMENDATIONS

We need recommendations on the appropriate use of fondaparinux in patients with ACS, as such recommendations are presently lacking, especially in rural areas, since they have few catheterization (CATH) labs and limited infrastructure besides limited interventional cardiologist coverage across the country (see Table 4).

The management of patients with STE-ACS starts early—with the first medical contact with emergency medical services. If STE-ACS is suspected, success in outcomes will depend on adequate pre-hospital care resources and prompt access to the healthcare facility. This requires efficient logistics and transportation, trained medical personnel, availability of therapeutics, and optimal communication with the healthcare providers in the affiliated hospital, enabling early activation of the CATH lab. In this context, educating primary healthcare physicians regarding the diagnosis and effective pharmacological management of ACS remains the mainstay of this protocol development.

## METHODOLOGY

One hundred and twenty cardiologists and interventional cardiologists who are national-level Key Opinion Leaders in Cardiology across India convened for two national and eight regional advisory board meetings from April to May 2022 to discuss the use of fondaparinux in the current management of ACS.

Recommendations and protocols were discussed for ACS management in rural healthcare

**Table 2** Summary of clinical evidence regarding antiplatelet therapy for the management of ACS

Study	N	Study drugs	Setting	Primary end point	Results
CLARITY [14]	3491	Aspirin + clopidogrel vs aspirin	STEMI with fibrinolysis	Occluded infarct-related artery on angiography or death or recurrent MI before angiography	15.0% vs 21.7%, OR = 0.64 [0.53–0.76]
CURRENT OASIS-7 [15]	25,086	Aspirin + clopidogrel (double dose for wk) vs aspirin + clopidogrel (standard dose)	ACS patients referred for an invasive strategy	Cardiovascular death, MI, or stroke at 30 d	4.2% vs 4.4%, HR = 0.94 [0.83–1.06]
TRITON-TIMI 38 [16]	13,608	Aspirin + prasugrel vs aspirin–clopidogrel	ACS patients undergoing PCI	Cardiovascular death, nonfatal MI, or nonfatal stroke	9.9% vs 12.1%, HR = 0.81 [0.7–0.90]
PLATO [13]	18,624	Aspirin + ticagrelor vs aspirin + clopidogrel	ACS patients	Death from vascular causes, MI, or stroke	10.2% vs 12.3%, HR = 0.84 [0.77–0.92]

centres that are equipped/not equipped with a CATH lab. These advisory boards were moderated by leading interventional cardiologists of the country, who discussed the recommendations below with a panel of advisors across the country.

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*Consensus statements introduced for panel discussion:*

1. Recommendations for the management of ACS in non-CATH-lab-equipped centres
  2. Recommendations for the management of ACS in CATH-lab-equipped centres
  3. What do the experts feel about bleeding in hospitals and its effect on morbidity and mortality within 1 month of ACS?
  4. Are there any patients who need post-procedural anticoagulation? Can fondaparinux be used?
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The recommendations given in this article are based on the advice of all the doctors who participated in the advisory board meetings, although physicians are free to choose a treatment independently based on their experience and at their sole discretion.

## PRACTICAL RECOMMENDATIONS

### Fondaparinux in the Management of ACS in Rural Non-CATH-Lab-Based Hospitals

#### *Recommendation*

Fondaparinux 2.5 mg, s.c. once daily should be used for medical management of ACS when PCI is delayed, denied by patients, unavailable, or contraindicated (Fig. 2).

*Summary:* Experts recommend administering a loading dose (2.5 mg) of fondaparinux for 8 days to patients with NSTEMI-ACS presenting at primary or secondary healthcare centres before transferring them to tertiary care centres within 8 h for angioplasty.

*Discussion of evidence:* In patients with NSTEMI-ACS who are not scheduled for PCI,

**Table 3** Summary of clinical trials of fondaparinux in the management of ACS

Study	N	Study drugs	Setting	Primary end point	Results
OASIS-5 [20]	20,078	Fondaparinux 2.5 mg and enoxaparin	ACS	Major bleeding through day 9	2.2% vs 4.1% ( $P < 0.001$ )
OASIS-6 [19]	12,092	Fondaparinux and UFH	STEMI	Composite of death or reinfarction	9 days: 7.4% vs 8.9% 30 days: 9.7% vs 11.2% ( $P = 0.008$ )
OASIS-6 subgroup analysis [21]	5436	Fondaparinux and UFH	STEMI patients receiving thrombolytics	Risk of severe bleeding Balance of benefit and risk (death, MI, and severe haemorrhage)	HR 0.62 (CI 0.40–0.94) HR 0.77 (95% CI 0.67–0.90)
RWE in Indian population [22]	611	Fondaparinux 2.5 mg OD	ACS	Bleeding events	0.98% during hospitalization 0.16% at 30 days ( $p > 0.05$ )
Comparative study [23]	40,616	Fondaparinux and LMWH	NSTEMI	Bleeding events	During hospitalization: 1.15 vs 1.8% 30 days: 1.4% vs 2.1%

fondaparinux is given for a few days after the third day of discharge. In patients with STE-ACS, fondaparinux can be used if primary PCI is not planned and in patients managed with thrombolytics or receiving no other form of reperfusion therapy. In patients thrombolysed with streptokinase, fondaparinux once daily is the preferred anticoagulant administered within 24 h (class IIA recommendation). In patients with STE-ACS, fondaparinux is useful when the window for thrombolysis is over [29].

### Recommendation

Fondaparinux 2.5 mg, s.c. OD highly preferred over enoxaparin in ACS management.

**Summary:** Cardiologists unanimously appreciated once-daily dosing of fondaparinux irrespective of body weight, unlike UFH/enoxaparin, which requires the monitoring of

coagulation parameters (PT, APTT, INR) and dose adjustments according to body weight. For patients receiving fondaparinux at a prophylactic dose (2.5 mg/day), it should be stopped 36–42 h before any neuraxial approach and may be resumed 6–12 h post procedure. If patients receive UFH, the initial management risk of bleeding is high, which is not an issue with fondaparinux; the doctors agreed that fondaparinux could be safely administered.

**Discussion of evidence:** The guideline recommends an initial dose of fondaparinux of 2.5 mg, i.v., and then 2.5 mg s.c. daily starting the day following hospitalization and lasting up to 8 days or until revascularization. Fondaparinux can be used as an adjunct to fibrinolytic therapy when there is any anticipated delay to performing primary PCI within 120 min. According to the recommendations of the ESC

**Table 4** Guideline recommendations for fondaparinux in patients with ACS

Guideline	Recommendation	Level of evidence	Reference
AHA/ACC-NSTEMI2014	Fondaparinux 2.5 mg s.c. for the duration of hospitalization or until PCI is performed	IB	[27]
AHA/ACC - STEMI 2013	Initial dose of 2.5 mg i.v., then 2.5 mg s.c. daily starting the following day for the index hospitalization up to 8 days or until revascularization. Contraindicated if CrCl < 30 ml/min	IB	[28]
ESC 2020-N-STEMI	Fondaparinux is recommended as having the most favorable efficacy–safety profile regardless of the management strategy. In patients on fondaparinux (2.5 mg s.c. daily) undergoing PCI, a single i.v. bolus of UFH (70–85 IU/kg, or 50–60 IU/kg in the case of concomitant use of glycoprotein IIb/IIIa inhibitors) is recommended during the procedure  Parenteral anticoagulation is recommended for patients undergoing peri-PCI, in addition to antiplatelet treatment, at the time of diagnosis and, especially, during revascularization procedures, according to the risks of ischaemia and bleeding	IB  IA	[25]
ESC-STEMI2017	Patient treated with streptokinase: fondaparinux i.v. bolus followed by an s.c. dose 24 h later  Fondaparinux is not recommended for primary PCI	IIA  IIIB	[29]

*ACC* American College of Cardiology, *AHA* American Heart Association, *ESC* European Society of Cardiology, *PCI* percutaneous coronary intervention

guideline (2017) regarding patients with STE-ACS treated with streptokinase, fondaparinux i.v. bolus can be administered after 24 h, followed by the fondaparinux s.c. dose. Fondaparinux is not recommended for early PCI intervention [21, 29]. The OASIS 5 trial showed that upstream fondaparinux therapy in NSTEMI-ACS patients undergoing early PCI is superior to enoxaparin in lowering severe bleeding by 50% while maintaining the same effectiveness [30].

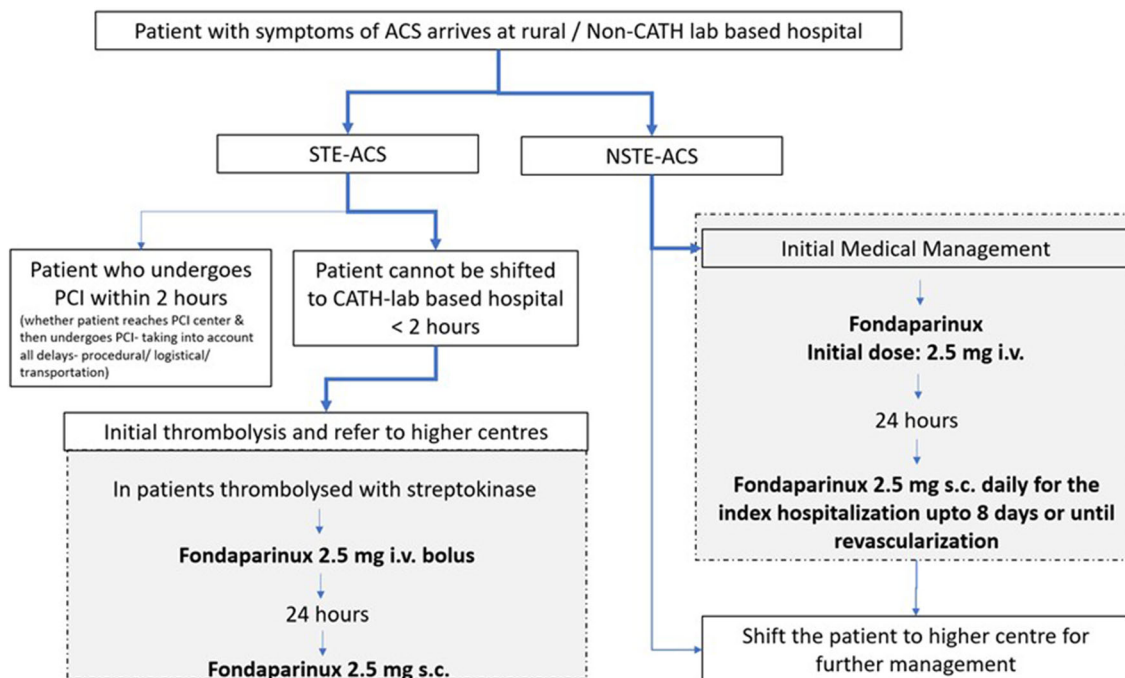
### Recommendation

Fondaparinux 2.5 mg IV bolus followed by fondaparinux 2.5 mg s.c. OD after 24 h should be recommended in STE-ACS patients, particularly in patients who are not undergoing primary PCI, in patients who receive no form of reperfusion therapy, or in patients who receive thrombolytic therapy (streptokinase), as it reduces mortality risk and reinfarction.

**Summary:** In patients thrombolysed with streptokinase, administer fondaparinux i.v. bolus followed by an s.c. dose 24 h later, which is given for 5 days. The experts recommend fondaparinux for 3 days after PCI, after which dual oral anticoagulant therapy (DAPT + NOAC) can be initiated. The experts do not recommend fondaparinux in primary PCI or in the CATH lab due to the possible risk of catheter thrombosis.

**Evidence:** In a subgroup analysis of the OASIS-6 trial, the role of fondaparinux as an adjunct to thrombolytic therapy in acute myocardial infarction was evaluated. The findings showed that in STEMI patients treated with thrombolytic agents (predominantly streptokinase), fondaparinux significantly reduced the risk of death, re-MI, and severe bleeds [21].





**Fig. 2** Recommendations for fondaparinux in patients with symptoms of ACS who arrive at a rural non-CATH-lab-based hospital. ACS acute coronary syndrome, i.v. intravenous, N-STE non-ST elevation, s.c. subcutaneous, STE ST elevation

### Fondaparinux in the Management of ACS in CATH-Lab-Based Hospitals

#### Recommendation

In patients with NSTEMI-ACS who received fondaparinux 2.5 mg OD before undergoing PCI, UFH 50–100 U/kg prior to PCI is recommended to prevent adverse outcomes like catheter-related thrombosis in the CATH lab (Fig. 3).

**Summary:** In patients with STE-ACS, fondaparinux can be given if primary PCI is not planned. If fondaparinux has already been administered before planning PCI, then within 4 h of PCI, UFH should be given inside the CATH lab to prevent the risk of catheter thrombosis. After initial thrombolysis, the preferred anticoagulant drug is fondaparinux.

**Discussion of evidence:** In patients with STE-ACS, fondaparinux can benefit patients in whom the window for thrombolysis is over. In OASIS-6, a higher rate of fondaparinux-related catheter thrombosis was largely avoided when UFH was used before PCI was performed. Thus, in patients undergoing non-primary PCI in

whom UFH was recommended before the procedure, there was no catheter thrombosis [20].

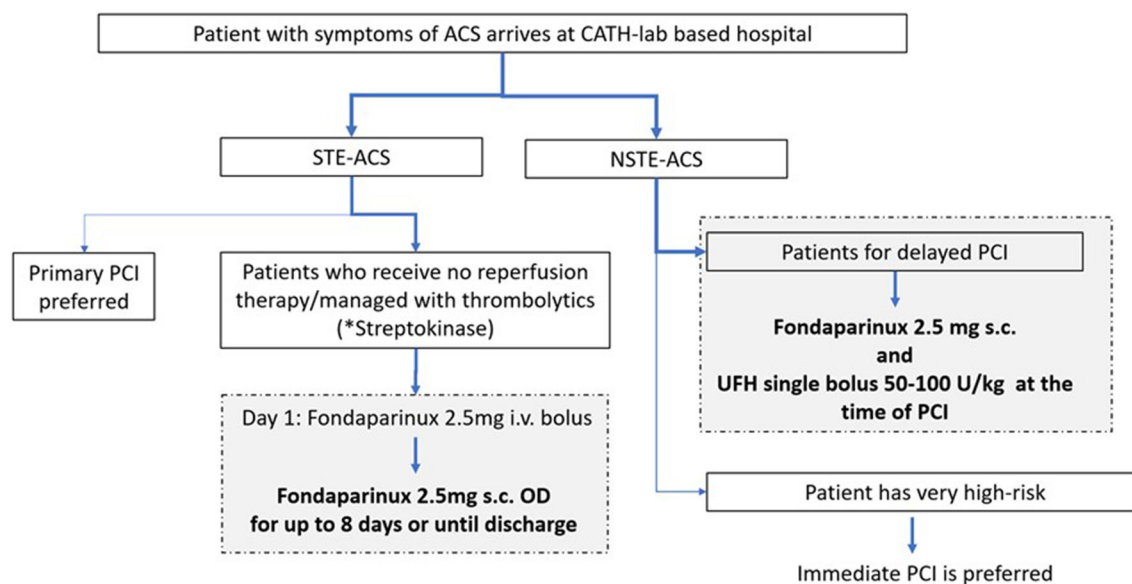
#### Recommendation

Fondaparinux 2.5 mg s.c. should be recommended for patients with NSTEMI-ACS who undergo early PCI, as it lowers severe bleeding while maintaining the same effectiveness as enoxaparin.

**Evidence:** The OASIS 5 study shows a reduced risk of bleeding on days 9 and 10; after that, it reduced ischaemic events and thus has a better net clinical outcome benefit than enoxaparin. There is no need to monitor coagulation parameters (like PT, APTT, INR) with fondaparinux, unlike enoxaparin, which requires continuous monitoring [20].

#### Assessment of Bleeding Risk

**Recommendation:** A detailed clinical history is essential for patients with comorbid conditions which increase their risk of a bleeding event when they are on anticoagulant therapy.



**Fig. 3** Recommendations for fondaparinux in patients with symptoms of ACS who arrive at a CATH-lab-based hospital. ACS acute coronary syndrome, N-STE non-ST

elevation, PCI percutaneous coronary intervention, s.c. subcutaneous, STE ST elevation

**Summary:** Most experts do not use any such bleeding risk scores in the clinical setting unless required as per the protocol for a clinical study. All experts agreed to develop a simple criterion to determine a high risk of bleeding based on the above factors rather than by using bleeding risk scores.

*A high bleeding risk is usually assessed clinically based on patient factors such as:* old age, female gender, weight less than 60 kg, thrombocytopenia, anaemia, liver impairment, renal impairment, on DAPT, and a history of using steroids or immunosuppressants.

**Evidence:** The ACUITY trial, conducted on a large scale, found that major bleeding complications had a significant adverse impact on the outcomes of patients with ACS who underwent early invasive management. These outcomes, including mortality, were independent of other factors. Additionally, there were several factors that were identifiable and independent predictors of major bleeding [31].

### Advantages of Fondaparinux over Other Anticoagulants

**Recommendation:** Fondaparinux 25 mg s.c. OD can be used in ACS individuals with renal impairment ( $\text{CrCl} > 30 \text{ ml/min}$  and  $\text{eGFR} > 20 \text{ ml/min/1.73m}^2$ ) and, with caution, in elderly patients above 60 years of age with no history of severe anaemia or renal impairment.

**Summary** Most of the experts agreed that in terms of efficacy, fondaparinux is similar to enoxaparin. However, compared with a heparin-based strategy (UFH or enoxaparin), fondaparinux reduces mortality, ischaemic events, and major bleeding across the full spectrum of ACS, and has a more favourable net clinical outcome in patients undergoing either an invasive or a conservative management strategy. Regarding safety, fondaparinux has a lower bleeding risk compared to LMWH. The experts discussed that fondaparinux is preferred over enoxaparin in elderly patients or patients with a high risk of bleeding, a history of bleeding, renal impairment, or thrombocytopenia.

**Evidence** Fondaparinux reduced the risk of death and re-infarction without increasing the risk of bleeding in STEMI patients. STEMI

patients who did not receive reperfusion therapy received the beneficial effects of fondaparinux [19]. In an OASIS-6 subgroup analysis of patients who received thrombolytic agents such as streptokinase, fondaparinux was found to significantly decrease the risk of death, re-infarction, and severe bleeding [21].

### Scope of Fondaparinux in Other Cardiac Conditions

*Recommendation* Fondaparinux is required in the post-PCI setting in the case of angioplasty, multiple stent implantation, atrial fibrillation, a large MI, or large thrombus formation.

*Summary* The panel discussed their in-depth clinical experience of using fondaparinux in their practice for other related cardiac conditions, such as in patients with atrial fibrillation, patients post-CABG, patients with a visible LV thrombus on ECHO, and patients with a residual thrombus post PCI. Since fondaparinux has a relatively low bleeding risk, it is a good choice for resolving LV clots and a large thrombus burden.

*Evidence* In a pilot study, fondaparinux was evaluated along with the standard treatment in patients undergoing echocardiography-guided cardioversion of atrial fibrillation. Fondaparinux appeared to be well tolerated and showed a similar efficacy to unfractionated heparin and vitamin K antagonist. A trend of greater thrombus resolution was also observed [32]. Fondaparinux also appears to be a safe alternative to heparin to prevent graft failure after CABG [33].

### CONCLUSION

The above recommendations and treatment protocol on the use of anticoagulants can help physicians manage patients with ACS at hospitals that are equipped with CATH labs and have cardiologists available and at hospitals without CATH labs or cardiologists. Fondaparinux is useful in non-CATH-lab-based hospitals for patients diagnosed with NSTEMI-ACS and STEMI-ACS patients who cannot be shifted to PCI-capable centres, or for patients who are thrombolysed at

peripheral centres. It is also recommended in CATH-lab-based hospitals if the patient is diagnosed with NSTEMI-ACS or STEMI-ACS and PCI cannot be performed or PCI is delayed.

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