The Diagnosis And Treatment Of STEMI In The Emergency Department

A 66-year-old man is wheeled into a community hospital's emergency department by EMS on a Saturday morning. He appears anxious, with beads of sweat on his forehead and pale skin. The paramedics indicate that the patient called 9-1-1 and reported chest pain that lasted for 30 minutes. They arrived on the scene 12 minutes after the call to find him doubled over. He described his discomfort as a "worse version of the pains that I've been having over the past few weeks," adding "I'm scared that I might be having a heart attack." The patient was given 325 mg of aspirin to chew at the scene and 2 sublingual nitroglycerin tablets that have not had any effect on his symptoms. Upon arrival, he is 55 minutes into this episode of chest pain. You have IV access, are providing him with supplemental oxygen, and have connected him to a cardiac monitor. The only lead shown is V2, and you see what look like depressions of the ST segment. You request a 12-lead ECG, and a clinical assistant begins to connect the leads. The nurse draws up basic labs, troponin I and CK-MB, and asks, "What would you like to do, doctor?" just as the 12-lead ECG prints out, showing 1.0- to 1.5-mm ST-segment elevations in leads II, III, and aVF. You are asking yourself the same question...

Acute myocardial infarction (MI) is the leading cause of death in the United States[1] and in much of the developed world. It is also a rising threat in developing countries.[2] Rapid diagnosis and treatment of MI is one of the hallmark specializations of emergency medicine (EM) because (1) emergency departments (EDs) are a common health care entry point for patients experiencing MI-associated

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CME Objectives

Upon completion of this article, you should be able to:
1. Manage STEMI in the ED setting using evidence-based practices.
2. Use a methodological approach to patients with chest pain who are at high risk of infarction.

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symptoms, (2) MI is a life-threatening condition, and (3) the emergency medical system has developed tools to manage it effectively. A patient whose MI is missed on evaluation has a 25% likelihood of a very poor outcome,[3] which makes this a "can't miss" diagnosis for the EM clinician. It is worth noting that missed MI has long been the most common justification for monetary awards in EM litigation.[3]

Acute coronary syndrome (ACS) is one of many causes of MI and describes cardiac ischemia that results when a blood clot, or thrombus, acutely narrows an artery supplying myocardial cells with blood. Specifically, ACS is ischemia due to atherosclerotic plaque rupture. Blood clotting factors interact with the plaque's contents and trigger the formation of a superimposed blood clot that narrows or, in the case of an ST-segment elevation myocardial infarction (STEMI), fully occludes the blood vessel lumen. ACS includes unstable angina and non-ST segment elevation myocardial infarction (UA/NSTEMI) as a combined phenomenon, as well as STEMI, but it is differentiated from other forms of cardiac ischemia such as demand ischemia or coronary vasospasm.

In UA/NSTEMI, a clot narrows the lumen enough to limit blood flow and cause myocardial ischemia. This ischemia often leads to chest pain or chest pain-equivalent symptoms (see the History section) of a different pattern from the patient's baseline experience. This can be chest pain of a different quality or frequency for a patient with a history of angina or new chest pain in a patient who has never experienced these symptom before. ECG changes may or may not be seen with ischemia alone. Ischemia may lead to infarction that involves the myocardial tissue but falls short of affecting the full thickness of the myocardial wall as is the case with STEMI. The infarction is evidenced by eventual elevation of cardiac enzymes (troponin and/or creatine kinase isoenzyme MB [CK-MB]) and ECG changes including ST-segment depressions, inverted T waves, or (the most common finding) non-specific ST-segment changes. (See Figure 1.)

In contrast, a STEMI typically occurs when this same process leads to complete occlusion of a coronary artery with transmural, or full thickness, myocardial wall infarction. (See Figure 1.) The ECG will show ST-segment elevations in the area of the heart fed by the affected blood vessel. Any ST-segment elevation is suggestive of a STEMI. However, ECG changes must meet STEMI criteria (see the Emergency Department Evaluation section) in order for this diagnosis to be made. [4-6]

In all cases of cardiac ischemia, treatment objectives are to increase the delivery of blood to myocytes beyond the obstructive lesion and to limit the myocytes' demand for oxygen-carrying and metabolite-removing blood. What differentiates STEMI therapy from treatment of other cardiac ischemic

Figure 1. Characteristics Of Myocardial Ischemia

Stable Angina	UA/NSTEMI	STEMI	Other MI
Chest pain[a]	Chest pain[a]	Chest pain[a]	(+/-) Chest pain
(-) ECG changes	Nonspecific ECG changes	ECG ST elevations[b]	(+/-) ECG changes
(-) Cardiac enzymes	(+/-) Cardiac enzymes	(+/-) Cardiac enzymes	(+) Cardiac enzymes
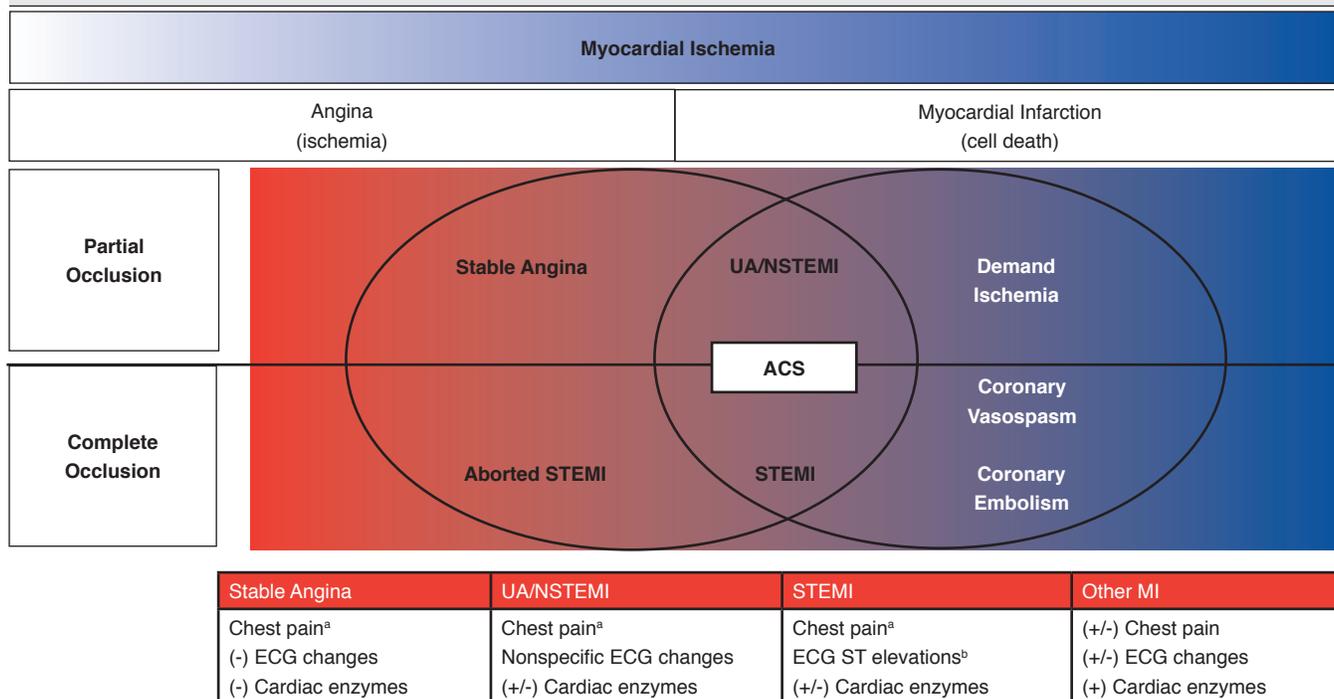
Abbreviations: ACS, acute coronary syndromes; ECG, electrocardiogram; MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction; UA/NSTEMI, unstable angina and non–ST-segment elevation myocardial infarction; [a] It is possible to have angina or myocardial infarction without chest pain. (See Common Pitfalls and Medico-Legal section.); [b] ST elevations must meet STEMI criteria in order to be diagnostic. (See Diagnosis section.)

Note: To view full color versions of the figures in this article, visit www.ebmedicine.net/topics.

conditions is the primary focus on immediate reperfusion with percutaneous coronary intervention (PCI) performed in a cardiac catheterization laboratory or with fibrinolytic agents given intravenously.[7]

Critical Appraisal Of The Literature

Ovid MEDLINE, the Cochrane Database of Systematic Reviews, and the National Guideline Clearinghouse were searched for articles relating to STEMI, with a focus on publications and consensus statements published after January 1, 2000. The references were then searched for related articles. Secondary references that were used by committees to develop consensus statements and guidelines were also reviewed. After the primary draft of this article was completed, focused follow-up literature reviews were conducted in August 2008 and March 2009 to identify articles published after the December 2007 release of the American College of Cardiology (ACC) and American Heart Association (AHA) Focused Update for the Management of Patients with STEMI.[8]

Cardiac Anatomy And MI Pathophysiology

As noted above, STEMI occurs when a thrombus forms in a coronary artery, completely occluding the vessel and preventing blood from flowing effectively to distal tissues. Under normal conditions, the depolarizing signal sent through the heart "zeros out" at the ST segment, which corresponds with the time between ventricular depolarization (the QRS complex) and ventricular repolarization (the T wave). As tissue dies, or infarcts, potassium leaks out of the cells, altering the charge over this portion of the heart. In the setting of ischemia, one may find a range of abnormalities including T-wave inversions and alterations of ST-segment levels and morphology. The change that is most specific to STEMI is an elevation of the ST segment on ECG results. This is due to transmural tissue infarction, which causes significant potassium leakage. The excess potassium creates a positive local tissue charge, reflected by the elevation of the ST segment.[9-11]

Blockage of particular coronary arteries leads to predictable regions of infarction. The pacer (or Purkinje) cells that run within these locations may also be involved. Death of Purkinje cells can create predictable rhythm disturbances.[12]

Identification of the anatomic distribution of ischemia and/or infarction is not an essential step in the diagnosis of a STEMI. It is important, however, to recognize that specific areas of infarction increase the likelihood of certain complications and that this information should be factored into treatment and monitoring decisions.[14]

Table 1 shows ECG changes and the associated major coronary artery branches, with the likely ana-

tomical areas of damage and potential complications of each. Matching ECG changes with the anatomy is helpful in mapping out the distribution of involved tissue by the presence of strain patterns (T-wave inversions, ST depressions) or infarction (ST-segment elevations with or without contiguous depressions). Caution should be taken when applying this concept in patients with severe coronary heart disease who are likely to have significant collateral circulatory flow. Rarely, congenital anatomical variations can also make it difficult to infer the distribution of damage and likely consequences.

Out-Of-Hospital Care

In the prehospital system, the management of patients with a suspected STEMI is driven by three goals: (1) delivering patients to an appropriate health care facility as quickly as possible, (2) preventing sudden death and controlling arrhythmias by using acute cardiac life support (ACLS) protocol when necessary, and (3) initiating or continuing management of patients during interfacility transport. Patients who arrive via an emergency medical services (EMS) transport vehicle often have already received some level of care. Basic life support ambulance crews are likely to have administered aspirin and oxygen, used an automated external defibrillator in the event of cardiac arrest, and obtained a basic history from the scene. Advance life support ambulances are additionally capable of providing nitroglycerin and ACLS protocol medications if necessary. Critical care transport vehicles have trained paramedics and nurses who are capable of providing intensive care–level management en route. In some EMS systems, 12-lead ECGs can be produced en route and the results sent to the receiving facility for evaluation before arrival. In regions where transport times are long, EMS teams may be trained and equipped to provide fibrinolytic therapy to STEMI patients before arrival without apparent contraindications. In areas with tertiary care centers within a reasonable distance, EMS teams may bypass small hospitals and deliver patients to facilities with PCI capability. (**See Controversies and Cutting Edge section.**) In addition, patients may be transported to or from a facility after fibrinolytic therapy for further management or when reperfusion is unsuccessful.

In all cases, direct sign-out from the EMS team to the treating emergency clinician is an important time-saving practice. A helpful checklist to get from the EMS team includes the following information.
1. The person who initiated EMS involvement (patient, family, bystander, transferring hospital) and why
2. Complaints at the scene
3. Initial vital signs and physical examination results, as well as notable changes

4. Therapies given prior to arrival and the patient's response
5. ECGs done at an outside hospital or en route, noting the context in which notable ECGs were printed
6. The patient's code status (if known)
7. Family contacts for supplemental information and family members who may be on their way to the ED, as they may be helpful in completing or verifying the history

Emergency Department Evaluation

Diagnosis

All patients with chest pain suggestive of ACS should have an ECG completed within 10 minutes of arrival at the ED and an early evaluation by an emergency clinician. Unlike most medical conditions, STEMI can be diagnosed with a single test before a patient's evaluation is complete.[18] Criteria for the diagnosis of STEMI have been proposed by the ACC/AHA and are in agreement with those of the European Society of Cardiology (ESC). The ACC/AHA and the ESC concur that STEMI exists when the ECG of the patient presenting with acute chest pain shows (1) ≥ 1-mm ST-segment elevation in at least 2 anatomically contiguous limb leads (aVL to III, including -aVR), (2) ≥ 1-mm ST-segment elevation in a precordial lead V4 through V6, (3) ≥ 2-mm ST-segment elevation in V1 through V3, or (4) a new left bundle branch block.[19] (**Figures 2 and 3.**) Laboratory tests, such as troponin and CK-MB measurements, are not a component of a STEMI diagnosis. However, they are helpful in the event that a STEMI is not diagnosed and other forms of MI are still suspected. (**See Figure 1, page 2.**) Every effort should be made to begin reperfusion immediately when ECG changes that are diagnostic for a STEMI are present.[20,21]

History

The patient's history should be taken while the ECG is being performed and initial therapies are being administered. Remember that time is myocardium. Ask the patient if he or she is having chest pain, when it started, what it feels like (stabbing, crushing, pressure, aching), and if it radiates to other parts of the body. Chest pain is the cardinal symptom of MI, but it is not always present, so be sure to ask about jaw/shoulder/neck/arm pain, dizziness, nausea, and shortness of breath. It is also important to elicit whether or not the patient has felt anything like this before, how it was similar or different, if he or she did anything that made it better or worse, or if he or she took anything at home to help with the discomfort. Information about past medical problems, past surgical procedures (when performed), medications taken (if the patient remembers), and any allergies is also helpful.

Historically, clinicians have been taught to review with these patients the major risk factors for cardiovascular disease: hypertension, known coronary artery disease, diabetes, hyperlipidemia, smoking, male sex, and an MI or early cardiac death in a first-degree family member before age 45 in men and 55 in women. Although colleagues in cardiol-

Table 1. Infarction Distribution With ST-Segment Elevation Myocardial Infarction And Consequences[4,15-17]

ST Elevations	Affected Coronary Artery	Area of Damage	Complications
V_1 through V_4	Left coronary artery: Left anterior descending	Anterolateral heart wall Septum Left ventricle His bundle Bundle branches	Left ventricular dysfunction: Decreased carbon dioxide, congestive heart failure Left bundle-branch block Right bundle-branch block Left posterior fascicular block Infranodal block (2° or 3°)
V_5 through V_6, I, aVL	Left coronary artery: Left circumflex branch	Left lateral heart wall	Left ventricular dysfunction: Decreased carbon dioxide, congestive heart failure Infranodal block (2° or 3°)
II, III, aVF, V_4R	Right coronary artery: Posterior descending branch	Inferior heart wall Right ventricle	Hypotension (particularly with nitroglycerin and morphine, which can decrease preload) Supranodal 1° heart block Atrial fibrillation/flutter, premature atrial contractions Infranodal block (2° and 3°) Papillary muscle rupture (murmur)
V_8 and V_9 (or ST depressions in V_1 and V_2)	90% Right coronary artery: Posterior descending branch 10% Left coronary artery: Left circumflex branch (will see elevations in V_5 through V_6)	Posterior heart wall	Hypotension Supranodal 1° heart block Infranodal block (2° and 3°) Atrial fibrillation/flutter, premature atrial contractions Papillary muscle rupture (murmur)

ogy and internal medicine may be interested in these details, they do not affect management in the ED. Active chest pain syndrome or a diagnostic ECG trump all other risk factors in a workup for MI. Time is best spent administering initial therapies and/or mobilizing resources for reperfusion.[25]

If the patient's ECG shows a STEMI, immediately ask about contraindications to fibrinolytic therapy, as this information will aid decisions about the appropriate reperfusion therapy. (**See Table 2.**)

Physical Examination

Aside from the vital signs, which are a critical dashboard in managing a STEMI or other ACS, a physical examination has limited usefulness in the diagnosis and initial treatment plan for patients with a STEMI. However, a focused physical examination can be

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Figure 2. STEMI Diagnostic Criteria[19,22,23]

American College of Cardiology/ American Heart Association ST-Segment Elevation Myocardial Infarction (STEMI) Diagnosis Guidelines

ST-Segment Elevation

In a patient presenting with active chest pain, a 12-lead electrocardiogram showing:

1. ST-segment elevation ≥ 1 mm (0.1 mV) in 2 or more adjacent limb leads (from aVL to III, including -aVR),
2. ST-segment elevation ≥ 1 mm (0.1 mV) in precordial leads V4 through V6,
3. ST-segment elevation ≥ 2 mm (0.2 mV) in precordial leads V1 through V3, or
4. New left bundle-branch block¥

Left Bundle-Branch Block

* Positive tests for cardiac enzymes troponin and creatinine kinase isoenzyme MB are helpful, but not essential. Therapy should not be delayed while awaiting results.

* Reciprocal depressions (ST depressions in the leads corresponding to the opposite side of the heart) make the diagnosis of STEMI more specific.

¥ *See the Special Circumstances section* for details on diagnosing STEMI in the setting of an old left bundle-branch block.

(ECG images from Brady W, Harrigan RA, Chan T. Section III: acute coronary syndromes. In: Marx A, ed-in-chief. Hickberger RS, Walls RM, senior eds. Rosen's Emergency Medicine Concepts and Clinical Practice. Part 3. 6th ed. St Louis, MO; CV Mosby; 2006:1165-1169.)

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helpful in identifying causes or complications of MI. If an ECG is diagnostic for a STEMI, the examination should be brief to evaluate for the signs listed in Table 3 (**page 8**) while the focus remains on initiating immediate reperfusion.

If the ECG is not diagnostic for a STEMI or other ACS condition, the examination can be more extensive. The information gathered can help emergency clinicians to sort through and prioritize items on the differential diagnosis.[25] However, it is important to note that even with the most careful evaluation, 1% to 5% of patients with an MI will have completely normal ECG results upon presentation.[26] In these cases, cardiac biomarker laboratory testing is helpful in identifying whether other forms of MI have occurred.

Differential Diagnosis

For patients presenting with acute chest pain, consider the following diagnoses:

- Aortic Dissection (AoD)
- Pneumothorax
- Pulmonary embolism
- Arrhythmia
- Myocarditis
- Pericarditis with or without cardiac tamponade
- Esophageal rupture or spasm
- Hypertensive urgency or emergency
- Gastroesophageal reflux disease
- Intercostal muscle strain
- Costochondritis

The predictive value of an ST-segment elevation on ECG is highly dependent on the incidence of the disease in the population into which the patient fits. For example, ST-segment elevations in a young person are less likely to be associated with MI because there is a lower incidence of MIs in younger populations. This fact, in and of itself, reduces the positive predictive value of the ECG as a diagnostic tool in this situation. For all patients, but particularly in the young, other causes of ST-segment elevation should be carefully investigated in the clinical context. (**See Table 4, page 8.**)

Initial Therapies

Much of what is considered standard of care for STEMI is based on the ACC/AHA guidelines, which are developed from a combination of the available evidence and consensus opinion amongst the guideline-writing group. In addition, the evidence for many common and emerging practices are controversial or under studied. For this reason, it is worth exploring these "initial therapies" in some detail.

Oxygen

Supplemental oxygen is given because of the theoretical benefit of maximizing oxygen delivery

Figure 3. Pathway For Diagnosis Of ST-Segment Elevation Myocardial Infarction

Patient presents with symptoms suggestive of a STEMI

↓

Perform ECG within 10 minutes

↓

Initiate IV access, monitor cardio-respiratory status, and perform history and focused physical examination.

↓

ST-segment elevation?

YES →

Meets STEMI diagnostic criteria?

NO →

Repeat the ECG; send cardiac biomarkers.

NO →

Any ECG changes?

YES ←

YES ↓

STEMI!

↓

Start Initial Therapies

Oxygen
Give to patients with oxygen saturation < 90%; use with caution in patients with congestive heart failure or COPD.

Aspirin
325 mg chewed, before or within 30 min of arrival

Nitroglycerin
0.4-mg SL tablets every 3-5 min up to 3 times; if effect is not sustained, can continue with an IV drip of 50 mg in 250-mL D5W, run at 10-20 mcg/min, then titrated to effect

Morphine
Still recommended by the ACC/AHA as an initial therapy; however, a notable 2005 trial found its use associated with increased mortality.[24] Give in multiple 2-mg doses and titrate upward, along with nitroglycerin, until patient is pain free.

↓

Provide fibrinolytics within 30 minutes or perform PCI within 90 minutes.

NO ↓

- Consider other ACS and non-ACS conditions.
- Repeat ECGs and reevaluate.
- Send and monitor cardiac enzymes.
- Conduct more extensive patient history and physical examination.

ACC/AHA, American College of Cardiology/American Heart Association; ACS, acute coronary syndromes; ECG, electrocardiogram; IV, intravenous; O₂, oxygen; PCI, percutaneous coronary intervention; SL, sublingual; STEMI, ST-segment elevation myocardial infarction.

in a patient with an ischemic condition. This was first recommended for myocardial infarction over 100 years ago.[117] However, there have been several studies dating back to the 1950s demonstrating concerning harmful effects.[118-120] Specifically, they have shown that when supplemental oxygen is given to non-hypoxic patients, it produces increased systemic vascular resistance and decreases cardiac output. In hypoxic patients, the data have varied between no effect to improvement.[121]

Our current practice is based on the first randomized controlled clinical trial done on the effects of oxygen therapy for MI patients.[122] It showed a reduction in MI-associated enzyme elevation, but these results did not achieve statistical significance (p=0.08). Given the small numbers involved in this study (n=151), it may have been underpowered to detect an actual clinical and/or statistical effect (type II error), but the results are not sufficient enough to support the routine administration of oxygen to all MI patients. In line with this evidence, the ACC/AHA's STEMI guidelines[62] only recommend supplemental oxygen for hypoxic patients. It is worth noting that all but one[123] of these studies were done before the advent of the pharmacologic agents, fibrinolytics, or PCI. In conclusion, the evidence is thin, and this highlights the need to re-consider the risks and benefits of oxygen therapy in both hypoxic and non-hypoxic patients, in the context of modern medical management of STEMI.[124]

Aspirin

Chewing an aspirin soon after the onset of symptoms has been shown to reduce mortality by 23%, as measured at 1 month after MI.[30] Aspirin is rapidly and maximally absorbed when chewed, and it takes effect in 60 minutes.[31] However, the benefits diminish greatly when aspirin is taken 4 hours after the onset of symptoms.[30] Over the years, dose recommendations have varied from 162 to 325 mg. Many studies have shown that the added bleeding risk associated with more than 162 mg of aspirin is minimal compared with the likely benefit, but a 2008 retrospective comparative study challenged this in the case of STEMI patients treated with fibrinolysis.[32] The authors concluded that the benefit of larger doses was outweighed by the proportionally increased bleeding risk in this subpopulation. If a patient is vomiting, aspirin can be given rectally with similar effect. A recent small study suggests that a 600-mg rectal suppository provides a sufficient level of salicylic acid within 90 minutes that meets or exceeds the level provided by standard doses of chewed oral aspirin.[33] If a patient has an aspirin allergy or significant active bleeding, a 300- or 600-mg bolus of clopidogrel can be given.[34] (**See the Special Circumstances section for more details.**)

Nitroglycerin

The vasodilatory effects of nitroglycerin increase blood flow to coronary arteries and help to alleviate spasmodic and ischemic pain.[35] In the pre-reperfusion era, early use was shown to limit infarct size and preserve ventricular function.[36] Nitroglycerin continues to be recommended for patients with a STEMI and active chest pain. However, the poten-

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Table 2. Fibrinolytic Reperfusion Contraindications

A. Absolute Contraindications

- Known structural central nervous system lesion (eg, arteriovenous malformation, primary or metastatic tumor)
- Any prior intracerebral hemorrhage
- Ischemic stroke within the last 3 months (excluding acute ischemic stroke within the last 3 hours)
- Significant closed head or facial injury within the last 3 months
- Suspicion of aortic dissection
- Active bleeding (excluding menses) or bleeding disorders

B. Relative Contraindications

- History of chronic, severe, and poorly controlled hypertension or severe hypertension (systolic blood pressure > 180 mm Hg or diastolic blood pressure > 100 mm Hg) on admission
- History of ischemic stroke within the prior 3 months
- Dementia or other known intracranial pathology not noted above
- Traumatic or prolonged (> 10 minutes) cardiopulmonary resuscitation or noncompressible vascular punctures within the last 3 weeks
- Major surgery within the last 3 weeks
- Internal bleeding within the last 3 to 4 weeks
- Pregnancy
- Active peptic ulcer disease
- Current use of anticoagulants (the higher the international normalized ratio, the greater the risk of bleeding)
- Prior exposure (> 5 days) or prior allergic reaction to streptokinase or anistreplase (if taking these agents)

(Adapted from 2007 ACC/AHA STEMI Treatment Guidelines.)

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tial benefits have to be balanced with the risks of hypotension and reflex tachycardia.

Morphine

Morphine blocks pain receptors and provides some anxiolysis, which is believed to reduce sympathetic tone and decrease myocardial metabolic demand. Its use has been a mainstay in the initial management of acute MI for decades. However, CRUSADE Initiative data, published as a 2005 case control study involving more than 17,000 patients, raised concerns that the use of morphine in patients with MI was associated with higher mortality. This excess mortality is believed to be attributed to morphine masking the symptoms of continued ischemia.[37] Despite the study's findings, morphine is still recommended as an initial therapy for STEMI by the ACC/AHA and the ESC, albeit with caution that the evidence for its use is less robust.[8]

Beta-Blockers

Beta-blockers reduce myocardial metabolic demand by decreasing heart rate and, to a lesser degree, myocardial contractility. Evidence supporting the use of beta-blockers in patients with acute MI arose from research demonstrating reduced rates of reinfarction and recurrent ischemia in those who received reperfusion therapy (fibrinolysis or PCI).[38,39] More recent evidence has shown that giving beta-blockers to all STEMI patients may lead to increased incidence of cardiogenic shock, which may outweigh the benefits.[40] In addition, a retrospective analysis of some older trial data failed to reproduce the previously reported benefits.[41]

The ACC/AHA currently recommends that an oral beta-blocker be given within 24 hours and that an IV beta-blocker is reasonable for patients who are hypertensive in the absence of (1) signs of heart failure; (2) evidence of a low cardiac output state; (3) post beta-blocker cardiogenic shock risk factors (age > 70 years, systolic blood pressure < 120 mm Hg, sinus tachycardia > 110 bpm or heart rate < 60 bpm, increased time since onset of symptoms of STEMI); or (4) other relative contraindications to beta blockade (PR interval > 0.24 s, second- or third-degree heart block, active asthma, or reactive airway disease). These recommendations are based on the results of COMMIT/CCS-2, a large randomized controlled trial that involved more than 45,000 patients.[8, 40] Oral beta-blockers do not need to be started in the ED, and the more selective use of IV beta-blockers is a change from prior recommendations and common practice, which categorize their use as an initial therapy for patients with acute MI.

Once a diagnosis of STEMI is made, these initial therapies should not delay the primary goal: to initiate definitive treatment with either fibrinolytic therapy within 30 minutes or PCI within 90 minutes. If the ECG does not meet the STEMI diagnostic criteria and the patient has ongoing ischemic symptoms, the test should be repeated at reasonable intervals along with continuous cardiac monitoring. These patients may develop a STEMI later in the symptom course.[9]

Definitive Treatment

Once a STEMI is diagnosed, the next immediate decision is whether to rapidly reperfuse the infarcting

Table 3. Signs To Look For During Physical Examination Of A Patient With Chest Pain

Sign	Concern
New murmur?	Papillary muscle rupture or acute valvular insufficiency
Jugular venous pulsation elevation?	Right-sided heart failure
Slowed capillary refill? Weak pulse?	Cardiogenic shock
Crackles or wheezes? Decreased breath sounds?	Congestive heart failure
Hemiparesis? Pulse differential between upper vs lower extremities or left vs right extremities?	Aortic dissection

Table 4. Alternative Causes of ST-Segment Elevations

Alternative Diagnosis	Clinical Context
Pericarditis/myocarditis	Fevers, recent radiation therapy
Benign early repolarization	Young, male
Left ventricular hypertrophy	Hypertension
Paced rhythm[27]	Pacemaker implanted
Significant hyperkalemia[28]	Renal failure
Coronary vasospasm	Cocaine or other stimulant use
Ventricular aneurysm	Prior infarction (usually associated with Q waves)
Spontaneous coronary artery dissection	Marfan or Ehlers-Danlos syndrome
Acute, severe emotional stressor	Takasubo cardiomyopathy

myocardium with fibrinolytic medications or with PCI via balloon angioplasty.

Fibrinolysis

Fibrinolytics are now widely available and easily accessible in most hospitals. The greatest benefit is derived when they are given within 1 to 3 hours after the onset of symptoms. Successful reperfusion rates range from 60% to 80%, but the chance of reperfusion success diminishes with time, even within this window.

The primary complications of fibrinolytics relate to excessive bleeding. Depending on where the bleeding occurs, it can also cause life-threatening problems such as large gastrointestinal tract bleeds, hemorrhagic stroke, and surgical wound dehiscence. As a result, a formal list of contraindications associated with an increased risk of hemorrhage has been compiled.[4] (**See Table 2, page 7.**) A patient with a yes response to any of the absolute contraindications in **Table 2A** is not a candidate for fibrinolysis. A yes response to any of the questions in **Table 2B** does not prohibit a patient from receiving fibrinolytic therapy, but it should raise significant caution in the mind of the deciding emergency clinician and weigh in favor of an alternative reperfusion plan.

The ACC/AHA guidelines recommend the initiation of fibrinolytic therapy within 30 minutes of a STEMI patient's contact with the medical system.[8] Reperfusion outcomes with this therapy, at 30 days post-intervention, are comparable to those with PCI when a patient has symptoms that are of short duration or when there is a low risk of bleeding or when achieving a door-to-balloon time of less than 90 minutes is not possible.[42] (**See Table 6, page 11.**) Most institutions have limited fibrinolytic options on their drug formulary. Emergency clinicians should know what options are available in advance and should be familiar with their specific characteristics and side effect profiles. (**See Table 5, page 10.**)

As noted earlier, once a fibrinolytic is administered, the complication of greatest concern is bleeding. The highest risk of bleeding occurs within the first 24 hours. Intracranial hemorrhage (ICH) is the most devastating complication. It occurs in less than 1% of patients[43] but carries a 55% to 65% mortality rate.[44] As a result, a computed tomographic (CT) scan of the head should be ordered for any post-fibrinolytic neurologic findings to rule out ICH. Also, all anticoagulants, antithrombotics, and antiplatelet agents should be held until ICH is ruled out.

Percutaneous Coronary Intervention

When available, prompt primary PCI in a cardiac catheterization laboratory is the preferred reperfusion option. If a facility has PCI capability, the STEMI should be reported as soon as the diagnosis is made, with a request to activate the catheterization labora-

tory emergently. (**See the Controversies and Cutting Edge section for more on this topic.**) When a facility lacks PCI capability, it may be feasible to coordinate a transfer (ambulance or helicopter transport) to another facility. In the process of identifying an accepting clinician for the transfer, a request should be made to activate the catheterization laboratory before the patient arrives. The goal is to have the patient achieve a door-to-balloon time of less than 90 minutes. The ability to achieve this goal should be incorporated into the decision of whether to use a fibrinolytic or a PCI.[50]

Fibrinolytics Versus PCI

The choice between fibrinolysis and PCI depends on the patient, the place, and the timing. Research on the relative effectiveness of fibrinolysis vs PCI has shown that the two modalities have comparable outcomes when PCI is not available within 1 to 2 hours and when contraindications to fibrinolysis are taken into consideration. Multiple clinical trials have shown that PCI, when available, has a higher rate of reperfusion and better short- and long-term outcomes than fibrinolysis.[50-53] A more recent study has shown that despite the ACC/AHA-endorsed time-to goal of 90 minutes, PCI may maintain superior outcomes for up to 150 minutes[49] For each patient, the decision should also take into account the duration of symptoms, the availability of the catheterization laboratory, the patient's mortality risk, any concerns that the STEMI might be of non-ACS origin, and the contraindications to fibrinolysis. (**See Table 6, page 11.**)

PCI And Fibrinolysis In Combination

One might think that following up the use of fibrinolytics with PCI would be a thoughtful choice for all STEMI patients. However, multiple randomized prospective trials have been unable to show a benefit of this approach.[54-56] Nevertheless, in *select* patients it is reasonable to consider PCI after fibrinolysis, in the form of facilitated PCI, rescue PCI, or follow-up PCI. The distinction between these therapies is subtle, but important.

Facilitated PCI

Generally speaking, PCI is the preferred method of reperfusion (especially for those who are in cardiogenic shock or are hemodynamically compromised) if it can be performed within 90 minutes of contact with the medical system. However, this "time-to" goal is not always achievable, particularly in facilities without PCI capability. As a result of this dilemma, researchers have sought to determine if administering fibrinolytics to initiate fibrinolysis during transport can *facilitate* reperfusion via PCI prior to arrival in the catheterization laboratory. However, a well-designed prospective multicenter study showed that when full-dose fibrinolytics were

given to all STEMI patients before PCI, the combination resulted in worse outcomes including increases in mortality, incidence of shock, reinfarction, need for urgent revascularization, and congestive heart failure.[57] The search is still on to see if facilitated PCI with less than full-dose fibrinolytics and some combination of antithrombotics will tip the balance toward favorable outcomes.

Given the limited evidence, the ACC/AHA 2007 updated guidelines do not recommend the use of full-dose fibrinolytics for facilitated PCI.[8] On the basis of data from the 2006 ASSENT trial (a randomized, controlled, prospective study involving 1667 patients),[58] the guidelines do advise that facilitated PCI with less than full-dose fibrinolytics can be considered in patients with a high mortality risk when PCI is unavailable within 90 minutes and in those who have a low bleeding risk (young age, controlled hypertension, and normal body weight).[8] A 2009 randomized controlled trial involving 1553 patients suggests that a patient whose door-to-balloon time is greater than 90 minutes but less than or equal to 150 minutes can be safely pretreated with glycoprotein IIb/IIIa complex (GPIIB/IIIa) platelet inhibitor and/or IV fibrinolytic therapy to achieve outcomes similar to those with primary PCI.[59]

Rescue PCI

Because reperfusion is not always achieved in patients who receive fibrinolysis, it is important to follow their response clinically and be prepared with an alternative plan in case of reperfusion failure.[60] Rescue, or salvage, PCI should be considered as a second attempt to achieve reperfusion in patients with (1) less than 50% resolution of ST-segment elevation in the most prominently elevated lead within 90 minutes, (2) persistent hemodynamically unstable arrhythmias, (3) persistent ischemic symptoms, or 4) developing or worsening cardiogenic shock after fibrinolytics. This can be done up to 24 hours after fibrinolysis, but it is not recommended for patients older than 75 years.[8]

Follow-up PCI

Follow-up PCI is done after primary fibrinolysis, when angiography identifies persistently narrowed coronary arteries that would benefit from angioplasty. The decision to perform follow-up PCI is rarely made within the ED. However, it is worth distinguishing this from primary PCI (door-to-balloon time < 90 minutes), facilitated PCI (a half dose of fibrinolysis with a GPIIB/IIIa agent), and rescue PCI (initiation of PCI after failed reperfusion from primary fibrinolysis).[61]

Adjuncts To Therapy

Important adjuncts to the treatment of STEMI include agents that prevent regeneration of coronary thrombi after patency has been established. The

Table 5. Characteristics Of Common Fibrinolytics For ST-Segment Elevation Myocardial Infarction[45-48]

Property	Alteplase (tPA) (Activase®)	Reteplase (Retavase®)	Tenecteplase (TNKase™)
IV Dosage	15-mg bolus, then 0.75 mg/kg over next 30 min (max of 50 mg), followed by 0.5 mg/kg over 60 min (max of 35 mg), for total dose of 100 mg	10-U bolus over 2 min, then another 10-U bolus also over 2 min (30 min later)	Weight-adjusted single bolus over 5 s < 60 kg: 30 mg 60-69 kg:35 mg 70-79 kg:40 mg 80-89 kg:45 mg ≥ 90 kg: 50 mg
Circulating Half-life	6 min	13-16 min	Initial half-life = 20-24 min Terminal half-life = 90-130 min
Route of Clearance	Liver	Liver and kidney	Liver
Antibody Formation	No	No	Yes, but rare (< 1%)
Risk of Intracerebral Hemorrhage	0.6%	0.8%	0.5%-0.7%
Reperfusion Rate by 90 min	79%	80%	80%
Lives saved per 100 persons treated	3.5	3.0	3.5

Abbreviations: IV, intravenous; tPA, tissue plasminogen activator.

2-pronged approach involves preventing thrombin generation and inhibiting platelet function.

Anticoagulants

The ACC/AHA guidelines recommend giving an anticoagulant to all STEMI patients for a minimum of 48 hours.[62] Unfractionated heparin (UFH), the traditional anticoagulant for acute MI, is given as a bolus of 60 U/kg (maximum of 4000 U) with a follow-up infusion of 12 U/kg per hour (maximum of 1000 U/hr) titrated to a targeted partial thromboplastin time (PTT) of 50 to 70 seconds. Enoxaparin (low-molecular-weight heparin [LMWH]) and fondaparinux are acceptable alternatives, with specific dosing regimens based on age and renal function. LMWH has the advantages of achieving a more consistent anticoagulation effect (so monitoring is usually unnecessary), a lower rate of heparin-induced thrombocytopenia (HIT) vs UFH, and convenience of administration. But LMWH is not without risks. Data from ExTRACT-TIMI 25, an international double-blind comparison of enoxaparin vs UFH in 20,506 patients enrolled in 48 countries, indicated that enoxaparin carries a slightly increased risk of bleeding.[8] It is also more difficult to reverse than heparin because it is not an infusion and has a longer half-life.

OASIS-6, an international randomized double-blind study comparing fondaparinux with control therapy (either placebo or UFH) in 12,092 patients enrolled in 41 countries, found that the bleeding risk with fondaparinux was lower than that for all of the other anticoagulants.[65] It is often the first-line anticoagulant in patients with HIT from prior heparin exposure, and administration is simplified with a fixed dose for all patients. The anticoagulant response is more predictable with fondaparinux than with heparin, allowing for less anticoagulation-level monitoring. However, this monitoring is done via anti-Xa levels, which are not performed in many hospital laboratories.[66] In addition, fondaparinux is not approved by the US Food and Drug Administration for this indication, and there is some literature showing an increased incidence of catheter tip thrombus when it is used in patients undergoing PCI.[67] For the dosages, advantages, and disadvantages of each of these agents, **see Table 7**.

Bivalirudin

Bivalirudin (Hirulog®, Angiomax®, Refludan®, hirudin-derived synthetic peptide) is a direct thrombin inhibitor that is available as an alternative to heparin therapy. It reversibly binds to the catalytic and substrate recognition sites on thrombin, which blocks circulating and fibrin-bound thrombin. Much like heparin, its full anticoagulation effect starts within minutes of administration, and once an infusion is stopped, it quickly diminishes with a half-life of 25 minutes.[68] Many studies done during the past 15 years have demonstrated greater reductions in ischemic outcomes with bivalirudin than with heparin, with a reduced risk of bleeding and other complications.[69-71]

The most recent ACC/AHA guidelines were published before the release of these data and offer bivalirudin as an option for use after initial heparin administration, but with class C level of evidence (consensus opinion or case study reports).[8] Results of the HORIZONS trial, a randomized multicenter comparative study of bivalirudin vs heparin with a GPIIB/IIIa agent, published in 2008, supported bivalirudin's lower rate of hemorrhagic complications, but noted an increased rate of in-stent thrombosis.[72] All of the patients were seen by an initial care team who diagnosed the patient's STEMI, started heparin, and requested urgent catheterization. Before catheterization was started, half of the patients had their heparin drip stopped and replaced with a bivalirudin drip/infusion. This study looked at bivalirudin use in the catheterization laboratory in a population who had received heparin prior to arrival. It was not designed to evaluate bivalirudin as an initial

Table 6. Choosing A Reperfusion Option For ST-Segment Elevation Myocardial Infarction

Fibrinolysis Favored	PCI Favored
• Catheterization laboratory not available • Inability to obtain central vascular access • Catheterization laboratory available, but without surgical backup • Inability to meet door-to-balloon time < 90 minutes • Door-to-balloon – Door-to-needle time > 1 hour	• Presentation > 3 hours after symptom onset • Catheterization laboratory available in-house • Patient with high mortality risk • Evidence of cardiogenic shock or significant hemodynamic compromise • Existence of significant relative contraindications to fibrinolysis • Uncertain STEMI diagnosis (inability to rule out other causes of ST-segment elevation or a left bundle-branch block with no prior electrocardiogram for comparison)

Abbreviations: PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

(Adapted from data in Antman EM, Hand M, Armstrong PW, et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2008;117(2):302-304.)

Table 7. Anticoagulants For ST-Segment Elevation Myocardial Infarction[8,66]

Drug	Dosage	Advantages	Disadvantages	Bleeding Risk
Heparin (UFH)	60-U/kg bolus (max, 4000 U), followed by 12-U/kg per hr infusion (max, 1000 U/hr)	Immediate anticoagulation Affects multiple sites in the coagulation cascade Long history of clinical use Its effect is easy to monitor via PTT Easy to stop anticoagulation by discontinuing the infusion ($t_{1/2}$ = 10 min)	Prevents free thrombin from activating, but does not inhibit clot-bound thrombin Nonspecific binding, so it has a variable anticoagulation effect requiring continued monitoring (PTT 50-70 s) Risk of HIT	Dependent on PTT level
Enoxaparin (LMWH)	Patients < 75 y with serum Cr < 2.5 mg/dL (men) or < 2.0 mg/dL (women): - 30-mg IV bolus, followed by - 1.0-mg/kg SC injection q12h Patients ≥ 75 y:- 0.75-mg/kg SC injection q12h Patients with serum CrCl < 30 mL/min: - 1.0-mg/kg SC injection every day	More effective thrombin inhibitor than with UFH More consistent anticoagulation effect, so it does not need to be monitored Lower risk of HIT than with UFH Long history of clinical use	Prevents free thrombin from activating, but does not inhibit clot-bound thrombin Less reversible than UFH Difficult to monitor Renally cleared Long half-life Risk of HIT	Highest
Fondaparinux	Patients with serum Cr < 3.0 mg/dL: 2.5-mg IV bolus for initial dose, then 2.5-mg SC injection every day, started 24 hr after	SC administration Once daily dosing Most consistent anticoagulation effect, so it does not need to be monitored Fixed dose for all patients No risk of HIT Does not cross the placenta Lower bleeding risk than with UFH or LMWH	Difficult to monitor (few laboratories can run anti-Xa levels) Long half-life Not approved by the US Food and Drug Administration Concerns about increased catheter tip thrombi in PCI patients	Lower
Bivalirudin	0.75-mg/kg IV bolus, followed by 1.75 mg/kg per hr Patients with CrCl < 30 mL/min: 0.75-mg/kg IV bolus, followed by 1.0 mg/kg per hr	Reduced risk of bleeding No risk of HIT Immediate anticoagulation Easy to stop anticoagulation by discontinuing the infusion ($t_{1/2}$ = 25 min)	Limited experience with its use No studies observing bivalirudin use without another anticoagulant either coadministered or used just beforehand Increased risk of in-stent thrombosis	Lowest

Abbreviations: Cr, creatinine; CrCl, creatinine clearance; HIT, heparin-induced thrombocytopenia; IV, intravenous; LMWH, low-molecular-weight heparin; PCI, percutaneous coronary intervention; PTT, partial thromboplastin time; SC, subcutaneous; $t_{1/2}$, half-life; UFH, unfractionated heparin.

anticoagulant, and prior heparin use in the experimental arm may be a confounding factor. As a result, this study's findings should not change emergency medicine practice. However, it is reasonable to discuss a transition to bivalirudin with the receiving cardiology team.

Antiplatelet Therapy

In addition to aspirin, which has been standard therapy for STEMI for 2 decades,[30,31,73] other antiplatelet agents have been used to further inhibit the formation of coronary thrombi.

GPIIB/IIIa Inhibitors: Abciximab (ReoPro®), Eptifibatide (Integrilin®), Tirofiban (Aggrastat®)

GPIIB/IIIa inhibitors are monoclonal antibodies or small polypeptides that bind to or compete with the platelet's GPIIB/IIIa receptor. This action inhibits cross-links with fibrinogen and further platelet aggregation. For STEMI patients who will be undergoing PCI, it is common practice to give a GPIIB/IIIa inhibitor (abciximab, eptifibatide, tirofiban) before or upon arrival in the catheterization laboratory to reduce the potential for clot formation.[8] However, the actual effect of GPIIB/IIIa inhibitors is not yet clear. Three major studies that examined their use in acute MI have shown improved coronary blood flow in the short term.[76-78] However, these and additional studies[79,80] have not shown long-term benefits and have demonstrated an increased risk of bleeding in patients older than 75 years. The risk vs benefit of using these agents in any particular patient should be discussed with the accepting cardiology team.

Thienopyridines: Clopidogrel (Plavix®)

Thienopyridines bind to the platelet adenosine diphosphate (ADP) $P2Y_{12}$ receptor to irreversibly inhibit activation and aggregation for the life of the platelet. An oral clopidogrel loading dose of 300 mg produces significant inhibition of ADP-induced platelet aggregation within 2 hours, with the maximal effect achieved in 6 to 15 hours, and is recommended in the ACC/AHA guidelines.[81] However, this practice does not provide a sufficient precatheterization antiplatelet effect for patients receiving primary PCI. Although it is not yet supported by clinical studies of STEMI, the pharmacodynamic profile of clopidogrel suggests that the antiplatelet effect begins earlier with larger loading doses (600 mg) than with the 300-mg dose and that this is a reasonable consideration for patients receiving primary PCI.[81-83] In situations where patients have a true aspirin allergy, clopidogrel can be used as a substitute. (**See the Special Circumstances section for more details.**)

However, many physicians hesitate to administer clopidogrel to STEMI patients who are undergoing primary PCI because clopidogrel can cause increased bleeding if coronary artery bypass grafting

is needed. Two randomized studies, the COMMIT/CCS-2 and the CLARITY-TIMI 28 trial (involving 45,852 and 3491 patients, respectively), examined the effects of clopidogrel use in STEMI patients and demonstrated that the drug has added value in those who are younger than 75 years and receive fibrinolysis with subsequent PCI or are unable to receive any form of reperfusion therapy.[84,85] As a result, the current ACC/AHA STEMI guidelines support the use of clopidogrel as a reasonable therapy in STEMI patients in these 2 subpopulations, but they do not comment on those undergoing primary PCI.[8] The 2007 ACC/AHA PCI guidelines more broadly support the use of clopidogrel before or during PCI in all STEMI patients despite the lack of studies showing a benefit in patients undergoing primary PCI.[86] With respect to bleeding risks, the need for an "emergent" CABG is a very rare phenomenon, and the increased bleeding risk can be averted by stopping clopidogrel 5 to 7 days before the surgical procedure.[87] As a result, it is not unreasonable to give a loading dose of 600 mg of clopidogrel before a STEMI patient is transported to a catheterization laboratory, as long as the evidence-based limitations of this therapy are understood.

Glucose Control

Clinical trials conducted in the early 1960s showed a significant reduction in mortality with the use of glucose-insulin-potassium (GIK) infusion in STEMI patients. This therapy was introduced in the 1960s to maximize potassium flux within ischemic myocardium as a means of reducing the incidence of arrhythmia, resolving ECG changes, and improving hemodynamics.[88-90] A large 2005 randomized controlled trial involving 20,201 patients across 3 centers evaluated the impact of GIK therapy in MI but did not reproduce these results. The study indicated that GIK infusions had no effect on mortality, cardiogenic shock, or cardiac arrest when given to all STEMI patients as a standard.[91] For this reason, routinely giving GIK infusions to STEMI patients is not advised. However, for patients with diabetes, early and tight glucose control with either an insulin sliding scale or an insulin drip is recommended by the ACC/AHA.[92]

Magnesium Repletion

Despite early interest, the routine administration of magnesium to patients with a STEMI does not appear to be indicated. Early trials noted improved outcomes when magnesium was routinely repleted in STEMI patients.[93] However, a later randomized, double-blind, controlled trial involving more than 6000 patients was unable to reproduce this effect in the broader study population or in any of the subgroups.[93] Nevertheless, magnesium was not found to be harmful and can be considered in patients with documented magnesium deficits who are on diuretic medications or are experiencing arrhythmias.[94]

Disposition

For STEMI patients undergoing PCI, a system should be in place to ensure catheterization laboratory activation as quickly as possible after diagnosis. When the laboratory is at another facility, activation should be coordinated as the patient is prepared for transfer. (**See the Controversies And Cutting Edge: Strategies To Improve Door-to-Balloon Time section.**) All STEMI patients who are not taken elsewhere for primary PCI should be admitted to a setting with a cardiac intensive care unit (ICU) as the destination of choice.

Special Circumstances

Old Left Bundle-Branch Block: Sgarbossa Criteria

A new left bundle-branch block (LBBB) in the setting of chest pain is a diagnostic criterion for STEMI. (**See Figure 2, page 5.**) It is indicative of a proximal left anterior descending artery, with the potential to damage a large section of the myocardium. The resistance of the left bundle branch becomes slow or does not occur at all, so the signal traveling down the right bundle branch ends up depolarizing the left bundle after it depolarizes the right ventricle. This delay and change in the electrical axis creates the characteristic ECG pattern. When there is a preexisting LBBB in a patient with chest pain, it can mask the ECG changes of a STEMI and delay diagnosis and treatment.

Decades of work have gone into determining how to diagnose a STEMI through an LBBB. One diagnostic tool that has gained widespread use because of its high specificity is the Sgarbossa Criteria. Identified and later validated in 1996, the Sgarbossa Criteria[95] contain 3 questions that can be used to identify a STEMI through an old LBBB. (**See Figure 4.**) To help in assessing the likelihood that a given patient with chest pain and a baseline LBBB is having a STEMI, a scoring system was developed that takes into account the probability of a STEMI with each criterion.
1. ST-segment elevation ≥ 1 mm in a lead with an upward QRS complex (5 points)
2. ST-segment depression ≥ 1 mm in V1, V2, or V3 (3 points)
3. ST-segment elevation ≥ 5 mm in a lead with a downward QRS complex (2 points)

Unlike the general STEMI criteria, the Sgarbossa Criteria do not need to be found in contiguous leads.

Criterion 1 is more indicative of a STEMI than is criterion 3, and the more criteria that are met, the more likely that a STEMI has occurred. According to the scoring system, a yes to question one is equal to 5 points, a yes to question two is equal to 3 points, and a yes to the third question is equal to 2 points. It is important to note that these criteria are not very sensitive, but they are highly specific. A score of 5 to 10 indicates an 88% to 100% probability of acute MI. With 0 points, there is still a 16% chance of a STEMI.

Aspirin Allergy Or Sensitivity

A 162- to 325-mg dose of aspirin taken early in the course of MI has been shown to produce a 23% reduction in mortality, measured at 1 month after the MI.[30] Patients with an aspirin allergy are at risk of losing this benefit. As a result, it is important to identify the allergic reactions of STEMI patients and determine whether the benefits of an aspirin outweigh the consequences of the reaction. For those in whom gastrointestinal tract bleeding is a concern, the cautious use of aspirin may be the better option. A 2005 randomized study involving 320 patients found the combination of a proton pump inhibitor and aspirin was a safer alternative than clopidogrel in patients who are at risk for gastrointestinal bleeding.[96] However, the CAPRIE trial, a randomized study involving 19,185 patients, demonstrated that substituting clopidogrel for aspirin was a sufficient antiplatelet inhibitor when compared with aspirin.[97,98] Thus, in

Figure 4. Flowchart For The Prediction of Acute Myocardial Infarction In The Presence Of Left Bundle-Branch Block[95]
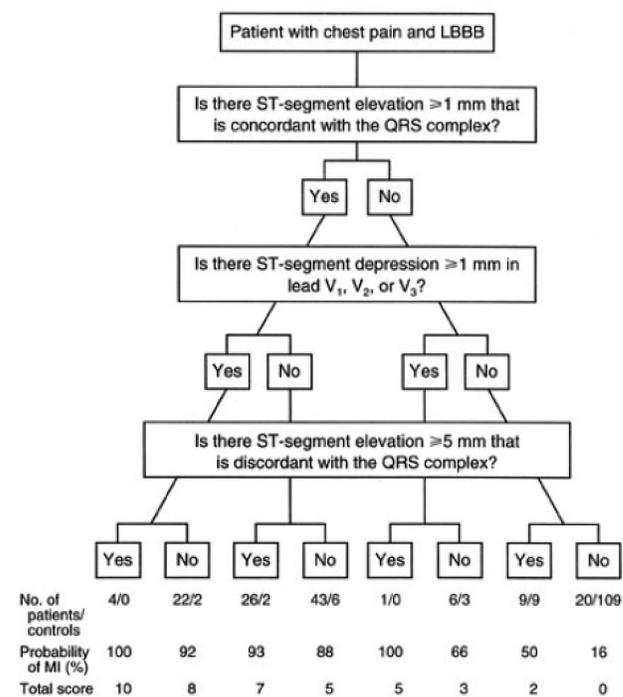
Abbreviations: LBBB, left bundle-branch block; MI, myocardial infarction. (Reprinted with permission. Copyright © 1996 Massachusetts Medical Society. All rights reserved.)

those patients with a definitive contraindication to aspirin (like angioedema or anaphylaxis), clopidogrel can be given as an alternative. In patients with other aspirin sensitivities, the reaction should be weighed against the cost of withholding therapy, and clopidogrel should be considered as a potent alternative. The current ACC/AHA guidelines do not comment on dosages, but keep in mind that in the acute care setting, higher loading doses of clopidogrel will be needed to approximate the platelet inhibition time-of-onset of aspirin for acute MI. As a result, a larger loading dose (600 mg or two 600-mg boluses 2 hours apart) may be most appropriate when clopidogrel is used as an aspirin substitute.[34]

MI With Aortic Dissection

The traditional teaching is that all acute MI patients should have a chest radiograph to screen for a wide mediastinum as an indication of possible AoD. Identifying AoD that presents at STEMI is important because fibrinolysis in these patients is associated with a mortality rate of 69% to 100%, often from cardiac tamponade or aortic rupture.[99,100] In general, 33% of patients whose AoDs are not diagnosed will die within the first 24 hours, 50% will die within 48 hours, and 75% within 2 weeks. Despite the high mortality, the case prevalence of AoD in the United States per year numbers in the thousands.

Ascending AoDs comprise about 50% of all dissections and are associated with a 7% to 13% incidence of retrograde dissection into a coronary ostium.[101,102] About 4% to 12% of this subpopulation of AoD patients will develop clinical and ECG findings compatible with acute MI.[103] However, STEMIs that are uncomplicated by AoD are orders of magnitude more common. In the career of any given EM clinician, far more patients with chest pain will be harmed by the delay in reperfusion than will be helped by early screening for AoD. As a result, routinely delaying reperfusion in STEMI patients in order to obtain a chest radiograph may not be appropriate general practice.

Decades of research have shown that a history of sudden onset of chest or back pain with or without syncope is the most sensitive tool in scaling the suspicion of AoD. Historical studies have shown that the sudden onset of chest pain alone has a sensitivity of 85%.[104] A study published in 2002 that used data from the International Registry of Acute Aortic Dissection and included 464 patients with confirmed AoD found that 95% reported pain in their chest, back, or abdomen; 90% reported it as severe or the worst pain they had ever experienced, and 64% described it as sharp. In addition, 72% of the patients had a history of hypertension.[105] Other data show that 75% of dissections occur in individuals 40 to 70 years of age, with the majority occurring in those 50 to 75 years old. There is a male to female predominance of 2:1 and

increased incidence with cocaine use. Forty percent of dissections in women younger than 40 years occur during pregnancy.[106] A pulse deficit, blood pressure differential (between right and left or upper and lower extremities), or focal neurologic defects may be concerning signs on physical examination. These characteristics are helpful when determining when to consider AoD as a complicating factor in STEMI patients.

In addition, chest radiography is unlikely to be the ideal method of screening. Although chest radiographs are easy to obtain, not all mediastinal widening observed on the radiograph is caused by dissection, and not all dissections will show a wide mediastinum on an x-ray. Other associated findings are often absent, and few are specific for dissection. More sensitive screening tests include a chest CT enhanced with IV contrast, magnetic resonance imaging, transesophageal echocardiography, transthoracic echocardiography, and angiography (the former gold standard), which has a sensitivity of 80% to 95%.[105] For experienced EM operators, a bedside EM cardiac ultrasound can be used as an extension of the physical examination. Transthoracic and transabdominal echos are not sensitive screening studies for AoD, but when an intraluminal flap is found, it can significantly raise the level of suspicion.

The investigation of dissection in the ED should be balanced with an awareness of the rarity of its occurrence, sensitivity to the historical and demographic factors that make it more likely, and consideration of how the delay to reperfusion can affect outcomes for STEMI patients.

Controversies And Cutting Edge

EMS Bypassing Smaller Hospitals For Those With PCI Capability

Primary PCI is preferred over fibrinolytic therapy in most STEMI patients, provided they make to it the catheterization laboratory of a PCI-capable facility within 90 minutes. Historically, individual EMS providers have chosen to bypass non-PCI facilities in favor of hospitals with PCI capability, but there have been concerns that this may lead to extended prehospital travel times that diminish the benefits of primary PCI over fibrinolysis. A 2006 study of US census data revealed that about 80% of American adults lived within 60 minutes of a PCI-capable hospital. Even more notable, for those whose closest hospital did not have PCI capability, 75% would have had less than an additional 30 minutes added to their transport time if taken to a PCI-capable hospital. There were notable geographic variations, but in most parts of the country, direct EMS transport can provide access to PCI.[107] Nevertheless, many centers are still struggling to meet door-to-balloon times for patients with far shorter EMS transports.

So until internal efficiency improves, allowing longer out-of-hospital times may lead to worse outcomes. In addition, a recent study compared facilitated PCI (with clopidogrel before catheterization laboratory intervention) occurring within 150 minutes to primary PCI and suggested similar outcomes.[58] This finding makes it more reasonable for EMS providers to stop at non-PCI centers for early evaluation and facilitating therapy before transporting a confirmed-STEMI patient to a PCI-capable center.

Facilitated PCI: Variable Definitions

The concept of facilitated PCI is difficult to understand because the term is used inconsistently in the literature. Most commonly, it refers to a number of antiplatelet agents and/or fibrinolytic combinations given before PCI. Most major studies have evaluated GPIIB/IIIa agents abciximab and eptifibatide independently and in combination with the fibrinolytics reteplase (Retavase®) and tenecteplase (TNKase™),

respectively. However, in one study the term facilitated PCI was used to describe the role of clopidogrel in situations better described as follow-up PCI, where PCI was done 2 to 8 days after primary fibrinolysis.[61] A more recent 2009 study used the term to refer to pretreatment with clopidogrel when door-to-balloon times for primary PCI were greater than the targeted 90 minutes but less than or equal to 150 minutes.[59] Awareness of the different definitions and the ability to characterize the definition used for any given study are important in appropriately interpreting the literature.

Improving The Sensitivity Of Occlusive Thrombi Diagnoses

The STEMI ECG diagnostic criteria were derived from data with the aim of developing a fast and highly specific test. However, studies have shown that despite a specificity of 97%, the criteria endorsed by the ACC/AHA pick up only 40% of ACS patients with completely occlusive thrombi.[14,108,109]

Common Pitfalls And Medicolegal Issues For STEMI

Missed MI is the leading reason for dollars awarded in closed malpractice settlements against EM practitioners. In addition, patients with a missed MI have a significant burden of morbidity and high mortality rates, which make this a major public health concern. The following pitfalls often lead to a missed STEMI.

- **Prolonged Time To Initial ECG**
  All patients presenting with chest pain should receive an ECG within 10 minutes of arrival. A STEMI cannot be diagnosed if a timely ECG is not performed.

- **Missed Atypical Symptoms**
  Failure to suspect STEMI in patients with atypical symptoms and chest pain equivalents (eg, shortness of breath, dizziness, nausea with or without epigastric discomfort) can lead to delayed diagnosis. Particular caution should be taken with women, the elderly, patients with diabetes, African Americans, and Hispanics, as these groups are known to present with atypical symptoms more often than others.

- **Improper ECG Interpretation**
  Memorizing the STEMI criteria is a first-line diagnostic tool for all EM practitioners.

- **Failure To Conduct Serial ECGs On Patients With Persistent Chest Pain**
  Because ECGs are snapshots in time, a single

tracing does not preclude the possibility that a STEMI occurred prior to presentation and has since resolved, nor does it catch those patients whose symptoms will evolve into a STEMI pattern over time. Although serial ECGs are recommended, along with continuous monitoring, as a way to gain a longitudinal view of a patient's condition (particularly patients with ongoing chest pain), it is a less-than-perfect strategy.

- **Delayed Care**
  Once a STEMI is diagnosed, rapid reperfusion is the primary treatment goal. The door-to goal can help set the pace while staff is mobilized to implement the initial therapies and start either fibrinolysis or transport to a catheterization laboratory for PCI. Outcomes are directly related to the amount of time that elapses between presentation and reperfusion.

- **Imbalanced Consideration Of AoD**
  Retrograde dissection of AoD into coronary artery ostia can cause a STEMI, but this is rare. The benefits of screening for AoD as the cause of MI should be balanced with the consequences of prolonged ischemic time from delayed reperfusion. Universally screening for AoD is not recommended, given that more patients will be hurt than helped by delayed reperfusion. The sudden onset of chest or back pain is 85% sensitive for identifying those at high risk of AoD as the cause of acute MI.

Even more concerning, the sensitivity of the 12-lead ECG is lower than 40% for complete vessel occlusion affecting the right ventricle or posterior myocardium or for a STEMI in the presence of an old LBBB.[110] Even with right-sided and posterior leads, the sensitivity of a 12-lead ECG is only moderately improved. As a result of misclassification or the time lapse until the ECG reflects the diagnostic pattern, lost myocardial tissue leads to worse outcomes.[111] Despite the limitations of the 12-lead ECG's sensitivity, its high specificity makes it an excellent tool for identifying patients who should receive immediate reperfusion therapy in the form of PCI or fibrinolysis.

Body surface mapping (BSM), or 80-lead ECG tracing, is a technique that uses multiple anterior and posterior chest leads to obtain a more complete picture of cardiac electrical activity. Multiple studies have demonstrated its effectiveness as a more sensitive and equally specific tool for distinguishing acute MI from ACS. A 2002 multicenter randomized clinical trial in 4 ED sites that evaluated patients with chest pain suggestive of ACS found the sensitivity of BSM for STEMI (90%-100%) to be far greater than the sensitivity of clinical suspicion for STEMI along with a 12-lead ECG (76%), an eventual troponin level elevation (57.1%), or an elevated CK-MB ratio (73%), while providing comparable specificity (95%-97%).[112] Efforts to develop this and other technologies in order to increase the detection rate and translation into clinical practice are continuing.

Strategies To Improve Door-To-Balloon Time

The importance of achieving prompt reperfusion for STEMI patients cannot be overemphasized. Achieving door-to-needle times is within the control of flow dynamics in an ED. However, achieving optimal door-to-balloon time requires coordination with individuals and services outside the department, any one of which can delay a patient from receiving prompt reperfusion.[113] The Centers for Medicare and Medicaid Services is aware of how minutes matter with STEMI. The agency tracks hospitals' achievement of door-to goals and considers a hospital's performance when evaluating it for reaccreditation. Several studies have examined communication and coordination links in the STEMI reperfusion chain to see which have made the biggest differences in reducing the time to reperfusion.[114,115] A study published in 2006 noted the most effective, but least used, strategies and observed that hospitals that used the greatest number of interventions had the shortest door-to-balloon times.[116] (**See Table 8.**)

Summary

STEMI is a "can't miss" diagnosis in EM. A methodological approach to patients with chest pain who are at high risk of infarction is the best tool in identifying this diagnosis.

Case Conclusion

In response to the nurse who asked what you'd like to do for your patient with chest pain and 1.0- to 1.5-mm ST-segment elevations in leads II, III, and aVF, you reply, "This patient is having a STEMI, so we need to focus on immediate reperfusion." EMS already gave a full aspirin, and the 3 doses of nitroglycerin the patient received en route had minimal effect on his pain. The physical examination is negative for crackles or rales, jugular venous pulsation elevation, or a heart murmur. The patient's pulses are bilaterally symmetric in his upper and lower extremities, and he has no evidence of extremity edema or neurologic deficit. The patient is scared but awake, alert, and oriented to person, place, and time. Your hospital does not have a catheterization laboratory on-site, and the nearest PCI-capable facility is 60 minutes away. Your nurse runs through a "fibrinolytic checklist." The patient has no absolute or relative contra-indications. You write an order for a heparin bolus, followed by a continuous infusion as well as tPA, and communicate this to the nurse, who has called a colleague into the room to help start the medications.

You then call the PCI-capable facility and speak with the EM clinician there about the patient. She explains that she can activate the catheterization laboratory while the patient is en route, but she calculates that "given the 60-minute lead time, the patient will not likely make a door-to-balloon time within 90 minutes." You note that the patient has no contraindications for lysis and that the heparin and tPA have just arrived in the room. You discuss the situation with the patient and his wife, who is now at his bedside. They express understanding of the risks and the benefits of rapid reperfusion via fibrinolysis vs tPA and consent to fibrinolysis, which is immediately

Table 8. Measures To Improve Door-To-Balloon Times[116]

Strategy	Time Saved (min)
Emergency medicine clinician activates the catheterization laboratory.	8.2
Single call to a central page operator activates the laboratory.	13.8
Emergency department staff activates the catheterization laboratory while the patient is en route to the hospital.	15.4
Staff members are expected to be in the catheterization laboratory within 20 minutes after being paged (vs 30 minutes).	19.3
An attending cardiologist is on-site at all times.	14.6
The hospital gives real-time feedback on the door-to-balloon times to the emergency department and catheterization laboratory staffs.	8.6

pushed. You watch as the ST-segment elevation on the monitor resolves. The patient's pain resolves in synch. The nurse prints out a 12-lead ECG to confirm. You call the PCI-capable facility to coordinate transfer for continued care in their cardiac ICU and possible follow-up PCI.

Note

Full color versions of the figures in this article are available at no charge to subscribers at www.ebmedicine.net/topics.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available.

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CME Questions

1. **ACS:**
   a. Is a term for all MIs
   b. Describes MI caused by clots that travel to the heart and block coronary arteries
   c. Characterizes a specific pathophysiological cause for MI involving atherosclerotic plaque rupture with the formation of a superimposed clot within a coronary artery
   d. Is a term that is no longer used when discussing STEMI

2. **A STEMI diagnosis can be made with:**
   a. An ECG and cardiac enzymes
   b. A history and physical examination with cardiac enzymes
   c. Cardiac enzymes alone
   d. An ECG alone

3. **STEMI diagnostic criteria require that a patient have chest pain or a chest pain equivalent and a qualifying ECG pattern. Which of the following is not a qualifying pattern?**
   a. ≥ 1 mm (0.1 mV) in 2 or more adjacent limb leads (from aVL to III, including –aVR)
   b. T-wave inversions
   c. ≥ 2 mm (0.2 mV) in precordial leads V1 through V3
   d. ≥ 1 mm (0.1 mV) in precordial leads V4 through V6

4. **When treating patients with chest pain and an ECG showing a STEMI, which of the following sets of questions is least important to ask?**
   a. Questions about the nature of their chest pain
   b. Questions about risk factors that increase the chance of an acute MI
   c. Questions about when and how their chest pain started
   d. Questions about potential contraindications to fibrinolytic therapy

5. **Other causes of ECG ST-segment elevation in patients complaining of chest pain include all of the following EXCEPT:**
    a. Pericarditis/Myocarditis
    b. Benign early repolarization
    c. Left ventricular hypertrophy
    d. Paced rhythm
    e. All of the above can cause ST-segment elevations

6. **In STEMI patients with documented or reported aspirin allergies:**
    a. The risks outweigh the benefits, so aspirin should be avoided
    b. The mortality benefits outweigh the risks, so aspirin should always be given
    c. Clopidogrel can be considered as an alternative
    d. Acetaminophen can be given as an alternative

7. **In patients with a preexisting LBBB and chest pain:**
    a. It is impossible to diagnose a STEMI with confidence.
    b. If a STEMI is present, it will be masked; therefore, all patients should be taken to the catheterization laboratory for coronary evaluation.
    c. The Sgarbossa Criteria have high sensitivity in identifying a STEMI.
    d. The Sgarbossa Criteria have high specificity in identifying a STEMI.

8. **The term facilitated PCI has been used to refer to:**
    a. Antiplatelet agents given before PCI
    b. Fibrinolytics given in combination with antiplatelet agents
    c. Fibrinolytics given before PCI
    d. All of the above

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May 2009 Errata

In the May 2009 issue of *Emergency Medicine Practice,* "Complications In Pregnancy Part II: Hypertensive Disorders Of Pregnancy And Vaginal Bleeding," question 2 was erroneously worded. To be more clear, the question should read: "Which of the following indicates severe preeclampsia?" As reworded, per Table 2 on page 3, answer "d" is correct; the other answers indicate mild preeclampsia. We apologize for any confusion.

- -

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EVIDENCE-BASED PRACTICE RECOMMENDATIONS

The Diagnosis And Treatment Of STEMI In The Emergency Department

Kosowsky, J, Yiadom, M. June 2009; Volume 11, Number 6

This issue of Emergency Medicine Practice focuses on managing STEMI in the ED setting using evidence-based practices. For a more detailed discussion of this topic, including figures and tables, clinical pathways, and other considerations not noted here, please see the complete issue at www.ebmedicine.net/topics.

Key Points	Comments
In all cases of cardiac ischemia, the treatment objectives are to increase the delivery of blood to myocytes beyond the obstructive lesion and to limit the myocytes' demand for oxygen-carrying and metabolite-removing blood.[7]	What differentiates STEMI therapy from treatment of other cardiac ischemic conditions is the primary therapeutic focus on immediate reperfusion with PCI in a cardiac catheterization laboratory or with fibrinolytic agents given intravenously.[7]
Unlike most medical conditions, STEMI is diagnosed with an ECG before a patient's evaluation is complete. The patient's history should be taken while the ECG is being performed and initial therapies are being administered.[25]	Remember that *time is myocardium.*
Diagnosing a STEMI requires a 12-lead ECG showing:[19,22,23] 1) ST-segment elevation: $\geq$ 1 mm (0.1 mV) in 2 or more adjacent limb leads (from aVL to III, including –aVR), or $\geq$ 1 mm (0.1 mV) in precordial leads V4 through V6, or $\geq$ 2 mm (0.2 mV) in precordial leads V1 through V3, or 2) A new left bundle-branch block	Positive tests for cardiac enzymes troponin and creatinine kinase isoenzyme MB are helpful but are not essential. Therapy should not be delayed while awaiting results. Reciprocal depressions (ST depressions in the leads corresponding to the opposite side of the heart) make the diagnosis of STEMI more specific.[19,22,23]
Upon arrival, initial therapies for a STEMI patient include aspirin, supplemental oxygen if oxygen saturation is < 90%, morphine, and/or nitroglycerin. In those patients with a confirmed STEMI, heparin should be added if there are no contra-indications.[8,30-37]	Caution should be used with morphine because of emerging evidence that its use increases mortality, as well as with nitroglycerin because of the risk of hypotension and reflex tachycardia.[8,35-37]
Initiation of reperfusion therapy is the primary focus when treating STEMI patients. This can be done via fibrinolysis (with a targeted door-to-needle time of 30 minutes) or with PCI (with a door-to-needle balloon time of 90 minutes).[8,49,50]	Reperfusion outcomes with fibrinolytic therapy, at 30 days post-intervention, are comparable to those with PCI.[42] The most appropriate intervention for any given patient is dependent on any contraindications to fibrinolysis, the ability to meet the door-to goals, the duration of symptoms, the presence of cardiogenic shock, and the patient's demographic risk of mortality.
The Sgarbossa Criteria takes into account the probability of a STEMI in patients with an old left bundle-branch block with each of the criterion:[95] 1) ST-segment -elevation $\geq$ 1 mm in a lead with an upward QRS complex (5 points) 2) ST-segment depression $\geq$ 1 mm in V1, V2, or V3 (3 points) 3) ST-segment -elevation $\geq$ 5 mm in a lead with a downward QRS complex (2 points)	Criterion 1 is more indicative of a STEMI than is criterion 3, and the more criteria that are met, the more likely that a STEMI has occurred. The Sgarbossa Criteria is highly specific but has low sensitivity; with 0 points, there is still a 16% chance of a STEMI.[95]

* See reverse side for reference citations.

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Noninvasive Ventilation Techniques In The Emergency Department: Applications In Pediatric Patients

It's that time of year again. The temperature is falling, respiratory viruses are multiplying by the minute, and your emergency department is at 160% capacity. You scan the white board at the start of your shift and note that almost half of the rooms are occupied by children with respiratory symptoms. Five children are receiving albuterol treatments for asthma exacerbations, and two of them are already on their second hour of continuous albuterol. You make a note to check on these patients promptly after receiving sign out from your colleague. Just as you are settling in for a long night, your triage nurse approaches you with a concerned look on her face. "Can you take a look at this kid, doc," she says. "I brought him straight back from triage. He's really tight." You rush to the room and encounter a 12-year-old anxious male in obvious respiratory distress. He's tachypneic and has both subcostal and supraclavicular retractions. Upon auscultation, you note inspiratory and expiratory wheezes with poor air entry. This is his third visit to the ED for wheezing this year. His last two visits resulted in PICU admissions. You quickly order continuous albuterol, ipratropium bromide, and IV steroids, as well as IV magnesium. Despite these interventions, his respiratory distress persists. A portable chest x-ray is performed and shows only hyperinflation. He's still tachypneic and retracting, and he can only speak in two-word phrases. You worry he may tire out, but knowing the risks of mechanical ventilation in children with asthma, you would like to avoid intubation if possible. What other options do you have?

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CME Objectives

Upon completion of this article, you should be able to:
1. Describe the potential advantages of noninvasive ventilation over endotracheal intubation.
2. Describe the various forms of noninvasive ventilation available for use in children.
3. Describe techniques for initiation of NIV in the emergency department.
4. Recognize the contraindications to noninvasive ventilation.
5. Summarize the current evidence relating to the use of noninvasive ventilation in children.

Respiratory distress is a common symptom in children and a common reason for visits to the emergency department.[1] Even for experienced emergency care providers, the management of respiratory distress in children can be challenging and frightening. While the great majority of children with respiratory distress will respond to standard therapies, including aerosols, suctioning, and supplemental oxygen, some patients will require a higher level of respiratory support. Endotracheal intubation and mechanical ventilation are critical interventions in many cases of respiratory failure, but there are definite risks associated with intubation. Children with asthma, in particular, are at high risk for complications, including pneumothoraces and pneumomediastinum.[2,3] In appropriately selected patients, noninvasive ventilation (NIV) may be an extremely valuable alternative to intubation.

NIV refers to the application of ventilatory support using techniques that do not require an invasive endotracheal airway. Multiple forms of NIV are available for use in children, including continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), intermittent positive pressure breathing (IPPB), humidified high-flow nasal cannula (HHFNC), and bi-level nasal CPAP. Use of NIV in pediatric patients is increasing in the emergency department, critical care unit, and prehospital environment, but what is the evidence supporting its use?

This issue of *Pediatric Emergency Medicine Practice* reviews the history of noninvasive ventilation, the rationale for its use, and the evidence supporting its use in children with acute and chronic respiratory failure. We will describe four modes in NIV currently available for use in children as well as techniques for initiation of each NIV device in the emergency department.

Abbreviations Used In This Article

ARF: Acute respiratory failure
CRF: Chronic respiratory failure
IPPB: Intermittent positive pressure breathing
CPAP: Continuous positive airway pressure
COPD: Chronic Obstructive Pulmonary Disease
PEEP: Positive end expiratory pressure
BiPAP: Bi-level positive airway pressure. (BiPAP is also the trade name for the device)
IPAP: Inspiratory positive airway pressure
EPAP: Expiratory positive airway pressure
NIPPV: Nasal intermittent positive pressure ventilation
NIV: Noninvasive ventilation
HHFNC: Humidified high-flow nasal cannula

History Of Noninvasive Ventilation

While most of the current NIV devices assist ventilation by providing positive pressure to the airways, the earliest NIV devices were actually external negative pressure ventilators, including the body ventilator and iron lung.[4,5] Negative pressure ventilators were widely used during the polio epidemics of the 1930s and 1960s, but these ventilators were problematic for several reasons. They were large and bulky, and they made access to patients difficult.[6] Alternative forms of respiratory support emerged during the 1970s and 1980s along with increased interest in noninvasive positive pressure ventilation.

Noninvasive positive pressure ventilation refers to the delivery of a pressurized gas to the airway via a nasal or full-face mask. Noninvasive positive airway pressure was first reported in the 1930s when researchers used continuous positive airway pressure to treat patients with acute pulmonary edema.[7] Another form of positive pressure ventilation, known as intermittent positive pressure breathing (IPPB), was introduced in the 1950s.[6] IPPB was initially used to provide a brief boost of positive airway pressure to patients with chronic respiratory failure. It was later used to deliver aerosolized bronchodilators to patients with chronic obstructive pulmonary disease (COPD) and asthma. IPPB use continued until the 1980s when several studies, including a prospective randomized trial sponsored by the National Institute of Health, failed to demonstrate an advantage of IPPB over aerosol treatment alone in patients with COPD.[8,9]

Following the introduction of the nasal CPAP mask, numerous reports of successful use of noninvasive positive pressure ventilation in patients with neuromuscular disease and chest wall deformities began to emerge.[10-14] Researchers demonstrated that nasal CPAP masks connected to positive pressure ventilators could provide nocturnal respiratory support in patients with neuromuscular disease. Additional advances in the early 1980s led to the routine use of CPAP in adult patients with COPD and pulmonary edema. More recently, NIV techniques have been used in pediatric patients with both chronic and acute respiratory failure.

State Of The Literature

The efficacy of NIV in adult patients with COPD and cardiogenic pulmonary edema has been clearly established. Multiple randomized clinical trials comparing NIV with conventional management of COPD exacerbations have shown reduced rates of endotracheal intubation and reduced mortality.[15-19] Similarly, several large randomized trials comparing NIV to standard therapy for cardiogenic pulmonary edema have reported improved oxygenation, decreased respiratory rate, and decreased need for intubation with the use of NIV.[20-22]

The efficacy of NIV in pediatric patients with

respiratory failure is less established. Most of the evidence supporting the use of NIV in children stems from retrospective reviews and case series, and many of these studies are limited by small numbers of participants, lack of blinding, and underlying disease heterogeneity.[23-29] Well-controlled randomized clinical trials comparing NIV techniques to conventional therapy in children are lacking. However, just recently, Yanez and colleagues published the first prospective randomized controlled trial (RCT) comparing NIV to standard therapy in 50 children with acute hypoxemic respiratory failure.[30] This study reported significant decreases in heart rates and respiratory rates within the first hour of treatment as well as a reduced rate of endotracheal intubation in the NIV group (28%) compared to the control group (60%; $p = 0.045$). While this randomized trial demonstrates efficacy of NIV in a heterogeneous population of pediatric patients with acute respiratory failure, further well-controlled trials are needed to determine the role of NIV in specific respiratory diseases, including asthma, bronchiolitis, pneumonia, and acute chest syndrome.

Pathophysiology And Mechanism Of Action

Noninvasive positive pressure devices deliver pressurized gas to the airway via a mask or nasal prongs. This results in an increase in mean airway pressure, which recruits atelectatic alveoli, improves respiratory gas exchange, and reduces work of breathing. (See **Table 1.**) In pediatric patients, NIV decreases work of breathing by unloading the diaphragm and accessory muscles and reducing inspiratory energy expenditure. NIV may also help stabilize the highly pliable chest wall in young infants, reducing retractions.[31] NIV provides positive end expiratory pressure (PEEP) which helps open collapsed alveoli, increasing functional residual capacity and improving oxygenation. NIV may also reverse hypoventilation by increasing tidal volume and minute ventilation in children with hypercapneic respiratory failure.[31] In children with occlusive apnea, noninvasive positive pressure may help reduce the number of occlusive events by maintaining upper airway patency.[32]

NIV may have negative physiologic effects, most of which are shared by invasive mechanical ventilation. Positive airway pressure increases intrathoracic pressure, which may decrease venous return and cardiac output in patients with poor cardiac function. In patients with normal cardiac function, NIV may actually improve cardiac output by decreasing left ventricular afterload.[33, 34]

Complications Of Endotracheal Intubation

Endotracheal intubation and mechanical ventilation are critical interventions in many cases of respiratory failure, but there are definite risks associated with intubation. Misguided tube placement may result in esophageal intubation or trauma to the upper airway. Airway trauma may lead to subsequent vocal cord dysfunction and subglottic stenosis. Additional risks during intubation include failure to intubate, aspiration, hypoxia, and increased intracranial pressure. Invasive mechanical ventilation may also cause infectious complications, including sinusitis and pneumonia.[35, 36] Ventilator-associated pneumonia has been reported in up to 10% of patients hospitalized in pediatric intensive care units.[34, 35] In children with asthma, endotracheal intubation may aggravate bronchospasm and greatly increase the risk of barotrauma.[2,3]

Advantages Of Noninvasive Ventilation

NIV has several significant advantages over endotracheal intubation. NIV devices leave the upper airway intact, decreasing the risk of airway trauma and preserving the natural defense mechanisms of the upper airways.[37, 38] Additionally, patients receiving NIV do not require paralytics, and the need for sedation is greatly reduced. Older children can communicate with their health care providers while receiving NIV. NIV is also less expensive than mechanical ventilation, and studies have shown that it decreases length of hospital stay and associated costs in adults.[39]

Noninvasive Ventilation Techniques And Equipment

There are several forms of NIV available for use in children, including continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), humidified high-flow nasal cannula (HHF-NC), and bi-level nasal CPAP. Each NIV technique is reviewed below.

Continuous Positive Airway Pressure

CPAP delivers a constant level of pressure support to the airways during inspiration and expiration. This constant pressure typically ranges from 5 to 10 cm H_2O and is delivered without regard to the respira-

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Table 1. NIV: Mechanisms Of Action

- Decreases work of breathing
- Increases functional residual capacity
- Recruits collapsed alveoli
- Improves respiratory gas exchange
- Reverses hypoventilation
- Maintains upper airway patency
- May increase or decrease cardiac output depending on underlying disease process

tory cycle. While pressures as high as 15 cm H_2O can be achieved, pressures above 15 cm H_2O are rarely needed. CPAP can be delivered through several different external interfaces, including oronasal masks, nose masks, nasopharyngeal prongs, single-nasal prongs, and short bi-nasal prongs. Oronasal masks (full-face masks) are commonly used in older children and adults, but these masks are not generally used in neonates and young infants due to the difficulty in maintaining an adequate fit and seal. Short bi-nasal prongs are now the preferred means of delivering CPAP to neonates and infants.[40] These short, wide prongs deliver equal pressure to both nostrils and have less resistance than the single-nasal prongs.[41]

CPAP can be provided by an airflow device designed specifically for this task or by a traditional full-capacity ventilator connected to an external interface. The free-standing infant CPAP device has a built-in flowmeter, which can be adjusted to achieve the targeted airway pressure. Airway pressure can be affected by several factors, including mask seal and air leak.

Nasal CPAP has been used extensively in premature neonates in the neonatal intensive care unit. Multiple studies have reported improved oxygenation, decreased work of breathing, and decreased obstructive apnea with this noninvasive ventilation device.[42-49] Nasal CPAP has also been used to treat infants with bronchiolitis and lower airway obstruction. Though nebulized aerosols are not routinely administered through the CPAP machine, there are reports of CPAP device modifications that allow delivery of aerosols.[50]

Bi-level Positive Airway Pressure

Bi-level positive airway pressure devices provide two levels of positive airway pressure during the respiratory cycle. A higher level of pressure is provided during inspiration (IPAP), and a lower level of pressure is provided during expiration (EPAP). The available IPAP range is 2 to 25 cm H_2O, with typical settings of 10 to 16 cm H_2O. The available EPAP range is 2-20 cm H_2O, with typical settings of 5 to 10 cm H_2O.[51] BiPAP can be delivered with a set respiratory rate or a back-up rate. Additionally, the cycle may be fixed as a function of time, or it may be triggered by the patient's inspiratory flow. As with CPAP, BiPAP may be provided by a machine specifically designed for this form of NIV or by a traditional ventilator set to appropriate bi-level pressure support settings. The level of pressure support in BiPAP is equivalent to the difference between the inspiratory and expiratory pressures (IPAP minus EPAP). Supplemental oxygen may be provided through the ventilatory tubing or directly through the mask. Many of the new BiPAP devices also have oxygen blenders.[51] It is also possible to give aero-

sols, such as albuterol and nebulized epinephrine, through the device.

Humidified High-Flow Nasal Cannula

Traditional nasal cannula gas flow in young infants is limited to 2 to 3 L/min due to mucosal irritation and dryness from the cool, dry air. High-flow nasal cannula devices deliver warmed humidified gas to the airways. Because the gas is nearly 100% humidified, nasal mucosal irritation is greatly reduced. This permits improved tolerance of high gas flow up to 8 L/min in infants and 40 L/min in older children and adults. Studies of high-flow nasal cannula in children are limited, but there are reports in the neonatal literature that indicate that HHFNC provides airway-distending pressure and respiratory support in preterm neonates comparable to nasal CPAP.[52,53] There are no known reports of aerosol administration through HHFNC devices. However, aerosols can be administered via a face mask while the nasal cannula remains in place.

Nasal Intermittent Positive Pressure Ventilation (NIPPV)

Nasal intermittent positive pressure ventilation is a relatively new form of NIV for infants that provides periodic increases in positive pressure above a baseline fixed pressure. NIPPV can be delivered via a nasal mask or nasal prongs connected to a ventilator, or it can be delivered by a free-standing device specifically designed for this form of NIV. Whereas the traditional infant nasal CPAP device contains a single flowmeter, the NIPPV device has a second flowmeter that periodically adds additional flow to the system. These periods of increased flow are known as "sighs" and can be delivered at a preset rate. The periodic increases in positive airway pressure may help offload the diaphragm and accessory muscles, decreasing the infant's work of breathing.

The device essentially provides two levels of CPAP, but unlike BiPAP, the infant cannot trigger the device to cycle between the high and low CPAP settings. These cycles are controlled by settings on the machine. Improved oxygenation can be achieved by increasing the amount of time on the high CPAP setting. Improved ventilation can be achieved by increasing the number of cycles between the high and low CPAP settings. Two Cochrane reviews of NIPPV in neonates have been published. One review reported that NIPPV may be beneficial in neonates with apnea of prematurity,[54] and the second review indicated that NIPPV may reduce rates of reintubation in preterm neonates after extubation.[55]

Initiation Of Noninvasive Ventilation In The Emergency Department

Patient Selection

In order to select appropriate candidates for NIV, several factors should be considered. These include the patient's underlying diagnosis, the specific cause of respiratory failure, and the potential for reversibility. When initiating BiPAP in particular, it is extremely important to select patients who are alert and cooperative. Many children will require coaching and reassurance when starting therapy. They may need time to become familiar with the mask and high air flow so that they do not work against the ventilator or fail a BiPAP trial prematurely due to anxiety. BiPAP is more likely to be successful when good patient-ventilator synchrony is established and a positive response to treatment (including decreased respiratory rate and decreased work of breathing) is seen within the first hour of treatment.[56] Patients with large air leaks, increased secretions, severe acid-base derangements, acute respiratory distress syndrome (ARDS), or persistent tachypnea are at high risk for NIV failure.[57-61] Prior to initiating NIV in any critically ill patient, it is important to prepare for potential NIV failure. Medications and equipment for endotracheal intubation should be readily available.

Contraindications To NIV

It is important to recognize the contraindications to NIV. Contraindications in children include apnea; impaired mental status; inability to handle oral secretions; poor cooperation or inability to tolerate the mask; hemodynamic instability; recent gastric, esophageal, or laryngeal surgery; and upper gastrointestinal bleeding.[31] (See **Table 2.**) NIV is also contraindicated if there is inadequate staff to monitor the patient appropriately.

Mask Selection

In infants and young children, selection of an external mask is dependent on the type of NIV to be used, as well as the age and size of the child. HHF-NC is generally provided via nasal cannula. Nasal CPAP and NIPPV in infants are generally provided via short, wide nasal prongs or a small nasal mask. In older children, CPAP and BiPAP can be provided via a larger nasal mask or a full-face mask. Nasal masks are often better tolerated in children because they create less anxiety and claustrophobia. Children with nasal masks are able to communicate with their caretakers and health care providers. The major disadvantage of the nasal mask is increased air leak though the mouth. This air leak may result in an inability to attain the desired IPAP. In critically ill children, full-face masks are generally preferred in order to minimize air leak and improve performance.[62]

Machine Settings

CPAP Settings

When initiating treatment with CPAP, start with low pressures (5 cm H_2O), and increase in increments of 1 cm H_2O as tolerated by the patient. Signs of a positive response to CPAP include a decrease in respiratory rate, improved oxygenation, and decreased work of breathing. Most nasal CPAP machines have an oxygen blender, and the FiO_2 can be adjusted via a dial on the flowmeter.

BiPAP Settings

Effective administration of BiPAP requires a well fitted mask and an alert, cooperative patient. BiPAP is most effective when good patient-ventilator synchrony is established. This requires a gradual bedside titration of IPAP and EPAP settings over a period of time. In order to avoid patient discomfort from high gas flow, BiPAP should be initiated with low pressure settings, which are then gradually increased over time. Maximum IPAP and EPAP are determined by the patient's diagnosis and level of comfort. It is reasonable to start with an IPAP setting of 8 to 10 cm H_2O. The IPAP should then be increased as needed to decrease the patient's work of breathing. IPAP levels of 10 to 16 cm H_2O are sufficient for most children, but levels as high as 20 cm H_2O can be used if needed. Levels above 20 cm H_2O may cause discomfort, and sedation may be required.[62] The EPAP is generally set at 2 to 4 cm H_2O initially, increasing to 10 cm H_2O if needed. This depends largely on the patient's diagnosis. Remember that the IPAP must always be higher than the EPAP by at least 2 cm H_2O to ensure appropriate flow. It is also important to ensure that the inspiratory time is appropriate for the patient. A tachypneic patient may require a reduced inspiratory time. If the inspiratory time (I time) is too long, then the patient may end up working against the machine in order to exhale.

While adequate coaching and a gradual increase in pressure settings will decrease anxiety in most patients, some children may require sedation to improve patient-ventilator synchrony. Moderately anxious pa-

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Table 2. Contraindications To NIV

- Apnea
- Impaired mental status
- Inability to protect the airway
- Excessive oral secretions
- Uncooperative or agitated patient
- Poor mask fit
- Hemodynamic instability
- Shock
- Upper gastrointestinal bleeding
- Recent gastric, esophageal, or upper airway surgery
- Inadequate staff to appropriately monitor patient

tients may be given a small dose of a benzodiazepine. In children with asthma, ketamine works particularly well due to its bronchodilatory effects. An initial loading dose of 0.5 to 1 mg/kg can be given, followed by an infusion of 0.25 mg/kg/hr.[51]

Humidified High-Flow Nasal Cannula Settings

HHFNC provides high-flow, nearly 100% humidified warmed oxygen via traditional nasal cannula. The warmth and humidification provided by the system permit delivery of high oxygen flow without irritation of the nose and mucous membranes, as well as more precise titration of the FiO_2 using oxygen mixers. The temperature is generally set at 35°C (95°F) to 37°C (98.6°F). In infants, the initial flow is set at 2 to 4 L/min and can be increased up to 8 L/min. In older children and adults, the flow rate can be increased to 40 L/min. The HHFNC device has an oxygen blender, and a dial on the machine can be used to adjust the FiO_2. When weaning a patient off HHFNC, one approach is to reduce the FiO_2 initially, followed by the flow. Once the FiO_2 is reduced to 30% and the flow is reduced to 2 to 3 L/min, the patient may be transitioned back to routine supplemental oxygen via nasal cannula.

Bi-level Nasal CPAP Settings

The bi-level nasal CPAP device provides two levels of CPAP, but the infant still breathes spontaneously with each phase. The low CPAP is initially set at 5 cm H_2O, and the high CPAP is initially set at 8 cm H_2O. These settings can be increased in 1 cm H_2O increments over time. The device has an oxygen blender, and a dial on the machine can be used to adjust the FiO_2. Oxygenation can be improved by increasing the amount of time the machine is in the high CPAP setting, and ventilation can be improved by increasing the number of cycles between the high and low CPAP settings.

Signs Of Effective Response To NIV

Patients must be observed carefully during the first two hours after initiation of NIV to assess clinical improvement, as well as signs of poor tolerance and worsening respiratory distress. A decreased respiratory rate is a fairly reliable sign of an effective response to NIV, regardless of the patient's diagnosis.[31, 61] Other signs of a positive response to NIV include improved oxygenation, decreased retractions and accessory muscle use, and reduction in the number of airway occlusion events in patients with obstructive apnea.[31] (See **Table 3.**) Improved lung volumes on chest radiographs as well as improved oxygenation on pulse oximetry and blood gases should also be noted. It is important to assess patients for signs of clinical improvement in the first few hours after initiation of NIV, but it is equally im-

portant to recognize when noninvasive techniques have failed. If patients have continued respiratory distress, poor oxygenation, excessive secretions, extreme anxiety, or hemodynamic instability, they should be intubated. (**See Table 4.**)

Indications For NIV In Children

Prehospital Care: NIV in Transport

Use of NIV is increasing in the prehospital environment. New transport ventilators offer more sophisticated ventilation modes, such as bi-level positive airway pressure and pressure-supported spontaneous breathing modes, which greatly enhance the ability to provide NIV during transport. These new ventilators also have more advanced monitoring and alarm features, increasing the safety of NIV during transport. The data on prehospital use of NIV is limited. There are several reports of improved dyspnea scores with the use of NIV during transport of adult patients with COPD exacerbations and congestive heart failure, but prehospital NIV in those reports had no effect on length of hospital stay or mortality.[63-66] Studies of NIV in pediatric transport are also limited. Several retrospective studies from the neonatal literature suggest that nasal CPAP is a safe method of respiratory support for transport of infants with respiratory distress,[67-69] but to the authors' knowledge, there are no published reports of prehospital use of NIV in older children. Further study of NIV in pediatric transport is needed to establish safety and efficacy in children.

NIV In Children With Chronic Respiratory Failure

The most well-documented application of NIV in children is in the treatment of chronic respiratory failure in patients with restrictive chest wall deformities and neuromuscular disease. Multiple case

Table 3. Signs Of Effective Response To NIV

- Decreased respiratory rate
- Decreased retractions and accessory muscle use
- Reduced airway occlusion events
- Improved oxygenation on pulse oximetry and blood gases
- Improved lung volumes on chest radiographs

Table 4. Reasons To Discontinue NIV

- Progressive respiratory distress
- Persistent tachypnea
- Persistent hypoxia despite supplemental oxygen
- Hemodynamic instability
- Vomiting
- Excessive secretions
- Increasing anxiety or agitation
- Increasing lethargy or worsening mental status

series have shown that NIV can effectively treat nocturnal hypoventilation and obstructive apnea in these patients.[70-73] Evidence suggests that the combination of NIV and pulmonary clearance may decrease the need for tracheostomy and improve long-term survival.[71] NIV has also been shown to be effective during acute deterioration of respiratory function during pulmonary infection in this patient population.[74, 75]

Noninvasive ventilation techniques have also been used to treat nocturnal hypoventilation and hypoxia in children with advanced cystic fibrosis. NIV has been shown to improve gas exchange during sleep to a greater extent than oxygen therapy alone in patients with moderate to severe disease.[76] NIV may also serve as a bridge therapy to facilitate survival before lung transplantation in children with end-stage cystic fibrosis.[77] However, the exact role of NIV in patients at various stages of the disease remains unclear. The benefits of NIV have largely been demonstrated in single-treatment sessions with small numbers of participants, and a recent Cochrane Database of Systematic Reviews review concluded that long-term RCTs were needed to determine the effect of NIV on pulmonary exacerbations and disease progression.[78]

NIV In Children With Acute Respiratory Failure

Pneumonia
RCT-level evidence for use of NIV in immunocompetent patients with community-acquired pneumonia is lacking in both adults and children. The published adult studies have shown inconsistent results, and the positive effects of NIV (decreased intubation rates and shorter ICU stays) have really only been clearly demonstrated in adult patients with underlying COPD.[79, 80]

Supporting evidence for use of NIV in pediatric patients with pneumonia is limited and stems primarily from retrospective case series[24, 25] and two small prospective studies.[29, 30] Fortenberry et al[24] described the use of bi-level positive airway pressure in 28 pediatric patients, aged 4 months to 17 years, with pneumonia and neurological disorders at high risk for respiratory failure. Both the respiratory rate and $PaCO_2$ fell after one hour of NPPV administration, and only three patients required intubation.

Padman et al[29] prospectively studied 34 children with impending acute respiratory failure and reported improved oxygenation and a reduced dyspnea score following treatment with bi-level positive airway pressure support. However, only 13 of the patients in this study had pneumonia. More recently, Yanez et al[30] published the first prospective RCT comparing NIV with standard therapy in 50 children with acute respiratory failure. This study included a heterogeneous patient population including children with asthma, pneumonia, and bronchiolitis. Only three patients had bacterial pneumonia. This study reported significant decreases in heart rate and respiratory rate within the first hour of treatment, as well as a reduced rate of endotracheal intubation in the NIV group (28%) compared with the control group (60%; p = 0.045).
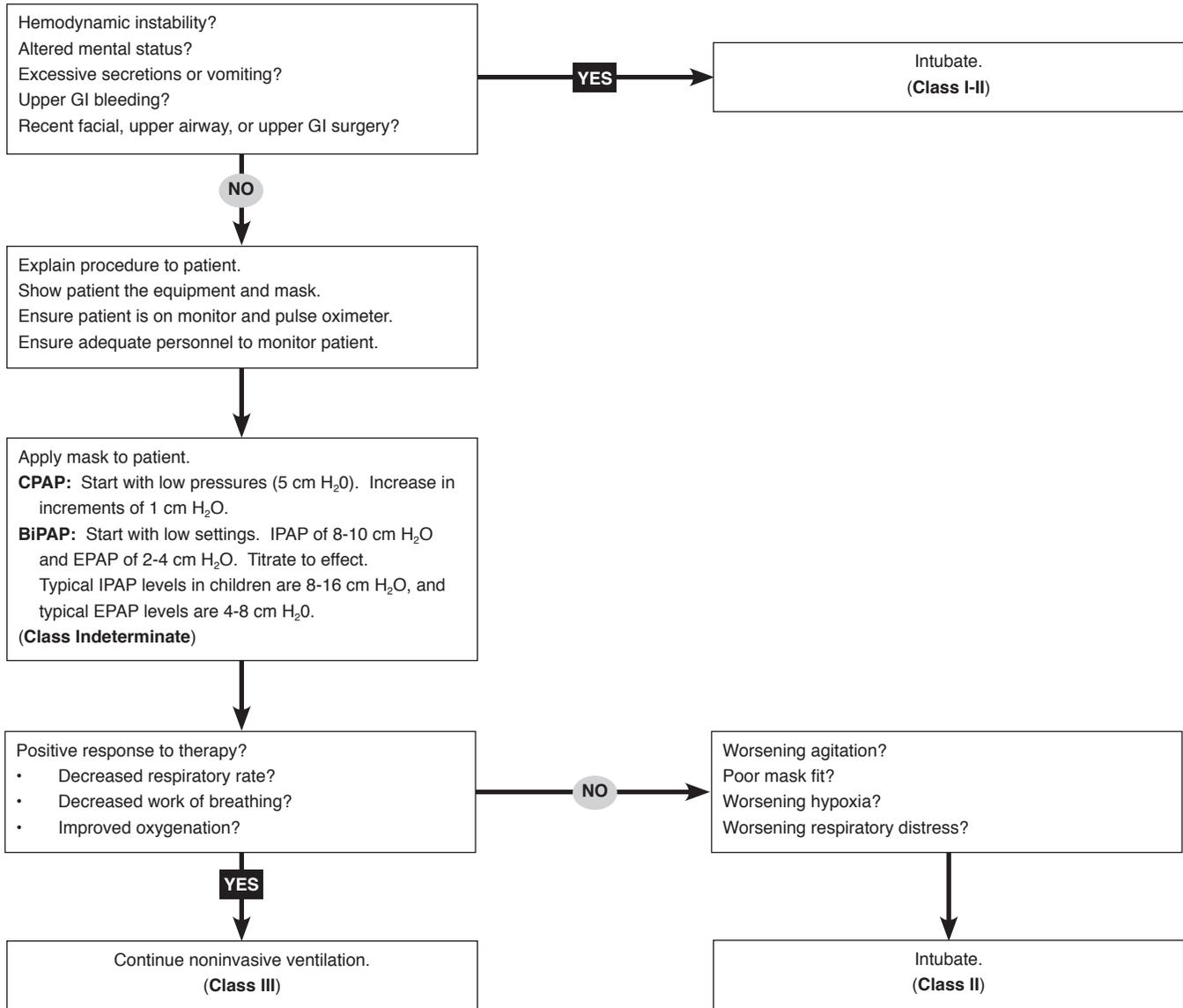
Asthma
There are increasing reports of successful use of NIV in children with status asthmaticus, but RCT-level evidence is not yet available. Teague et al[27] described the use of bi-level positive airway pressure in the treatment of 26 children with status asthmaticus complicated by severe hypoxemic respiratory failure. Nineteen patients had improved oxygenation following initiation of BiPAP, but seven patients required endotracheal intubation. Beers et al[81] examined the benefit of BiPAP in conjunction with beta-2 agonist therapy in 83 pediatric patients with status asthmaticus in the pediatric emergency department and found that 88% had improved oxygenation and 77% had decreased respiratory rate. Only two patients in this study required intubation. Thill et al[82] performed a prospective randomized crossover trial of bi-level positive airway pressure and standard therapy in 20 children with lower airway obstruction and found a significant decrease in the respiratory rate and a lower asthma score in all children during NIV.

Bronchiolitis
There are increasing reports of successful use of NIV in infants with bronchiolitis, but many of the studies are limited by heterogeneous patient populations and a small number of patients with bronchiolitis. As with asthma, RCT-level evidence is not yet available. Javouhey and colleagues[83] recently published a retrospective review that focused on the use of NIV in children less than 12 months in age with bronchiolitis. They compared two cohorts of infants during two bronchiolitis seasons. During the first winter, invasive ventilation was the only support employed. During the second winter, NIV was used as the primary ventilatory support. The authors reported significant decreases in ventilator-associated pneumonia and duration of oxygen requirement in the NIV cohort. Two additional studies by Martinon-Torres and colleagues[84, 85] also focused on infants with bronchiolitis. However, the primary aim in each study was to evaluate the effects of heliox in combination with nasal CPAP in infants with severe, refractory bronchiolitis. The authors reported significant improvements in a clinical score (Modified Wood's Clinical Asthma Score), transcutaneous CO_2, and arterial oxygen saturations in infants treated with both heliox-nasal CPAP, as well as oxygen-

Clinical Pathway: Noninvasive Ventilation in Children

Hemodynamic instability?

Altered mental status?

Excessive secretions or vomiting?

Upper GI bleeding?

Recent facial, upper airway, or upper GI surgery?

YES →

Intubate.
(**Class I-II**)

NO ↓

Explain procedure to patient.

Show patient the equipment and mask.

Ensure patient is on monitor and pulse oximeter.

Ensure adequate personnel to monitor patient.

↓

Apply mask to patient.

CPAP: Start with low pressures (5 cm H_2O). Increase in increments of 1 cm H_2O.

BiPAP: Start with low settings. IPAP of 8-10 cm H_2O and EPAP of 2-4 cm H_2O. Titrate to effect. Typical IPAP levels in children are 8-16 cm H_2O, and typical EPAP levels are 4-8 cm H_2O.

(**Class Indeterminate**)

↓

Positive response to therapy?
- Decreased respiratory rate?
- Decreased work of breathing?
- Improved oxygenation?

NO →

Worsening agitation?

Poor mask fit?

Worsening hypoxia?

Worsening respiratory distress?

YES ↓

Continue noninvasive ventilation.
(**Class III**)

↓

Intubate.
(**Class II**)

Class Of Evidence Definitions

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Class of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Class of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case control studies
- Less robust RCTs
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Class of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Class of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and represen-tatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA.* 1992;268(16):2289-2295.

nasal CPAP. However, an improvement in clinical scores and a decrease in CO_2 were greater in the heliox group.[85] None of the infants required endotracheal intubation.

Acute Chest Syndrome

NIV has also been used in patients with sickle cell disease presenting with acute chest syndrome, but the evidence is very limited. Padman[28] reported on the use of bi-level positive airway pressure in 25 occurrences of acute chest syndrome in children aged 4 to 20 years and reported significant decreases in respiratory rate, heart rate, and oxygen requirements following initiation of NPPV.

Immunocompromised Children With Respiratory Distress

NIV may have a particularly important role in the treatment of immunocompromised children with respiratory distress. While the pediatric evidence is limited, multiple adult studies, including several RCTs and a systematic review, have confirmed the benefit of NIV in immunocompromised adult patients with acute respiratory failure.[86-89] These adult studies consistently report improvements in gas exchange, reduced rates of intubation, decreased ICU stays, and decreased ICU mortality in immunocompromised patients treated with NIV.

Evidence supporting the use of NIV in immunocompromised children is limited to small case series and retrospective reviews.[90-92] In the largest review to date, Pancera and colleagues[92] reviewed 239 cases of respiratory failure in immunocompromised children over an eight-year period and reported an NIV success rate of 74%. Multivariable analysis showed that cardiovascular dysfunction and solid tumors were independent predictive factors for NIV failure.

While the adult literature strongly supports use of NIV in immunocompromised patients with acute respiratory failure, pediatric RCT-level evidence is not yet available.

Complications Of NIV

NIV is generally much safer than endotracheal intubation, and the rate of complications is low. Patients receiving NIV may avoid many of the risks associated with intubation including upper airway trauma, esophageal intubation, and ventilator-associated pneumonia as well as post-extubation complications such as subglottic stenosis and vocal cord dysfunction.[35] There have been very few reports of major adverse events in children. Minor complications at the interface margin are relatively common and include skin irritation, nasal bridge pain, mucosal dryness, and eye irritation.[56] Poorly fitted nasal masks in neonates may also result in nasal ulceration over time.[56] Major systemic complications are rare but have included gastric insufflation, barotrauma (including pneumothorax and pneumomediastinum), depressed cardiac output, and progressive hypercarbia.[62] The most common complication is failure of the technique. Children receiving NIV require close monitoring, especially during the first 2 hours after initiation of treatment. These children should be placed on continuous pulse oximetry as well as cardiac monitors. End-tidal CO_2 monitoring should be strongly considered. Frequent reassessment by nursing staff and respiratory therapists is required to assess for signs of clinical improvement as well as for signs of worsening respiratory distress.

Summary

Use of noninvasive ventilation is increasing in the emergency department and prehospital environment. In appropriately selected patients, NIV may have several advantages over endotracheal intubation. NIV techniques leave the upper airway intact, decreasing the risk of airway trauma and nosocomial infections. Patients receiving NIV generally require less sedation and are able to communicate with their health care providers during treatment.

Children may require reassurance and coaching prior to initiation of NIV in the emergency department. NIV also requires experienced respiratory staff and nurses who are able to closely monitor the patient, particularly during the first hour after initiation of therapy.

Reports of successful applications of NIV in pediatric patients continue to increase in number, but RCT-level evidence is limited. While the future of NIV in pediatric patients is very promising, further investigation and well-organized clinical trials are needed to clearly establish the safety and efficacy of NIV in children.

Case Conclusion

You consider a trial of bi-level positive airway pressure for this patient and ensure that he is an appropriate candidate for NIV. His mentation and vital signs are reassessed. Though he can only speak in two-word phrases, he is alert and answers questions appropriately. He is well perfused with a good pulse and a normal blood pressure for his age. You decide that he is a good candidate for BiPAP. He is already on a full cardiorespiratory monitor and continuous pulse oximetry. You verify that there is adequate respiratory support staff to provide close monitoring of this patient. After explaining to your patient that you are going to apply a mask that will help him to breathe, you allow him to become familiar with the mask and airflow. Therapy is initiated, beginning with low settings, including an IPAP of 10 cm H_2O and an EPAP of 5 cm H_2O. Since your patient

Risk Management Pitfalls For Noninvasive Ventilation

1. **"This patient required intubation for severe asthma last year, so we shouldn't waste time with a trial of noninvasive ventilation."**
Endotracheal intubation in children with asthma is associated with many complications, including barotrauma, air trapping, pneumothorax, and pneumomediastinum. Intubation in patients with asthma should be avoided if possible. If the patient with status asthmaticus is hemodynamically stable with a normal mental status, a trial of NIV should be strongly considered prior to intubation. While the patient with severe asthma will need close observation and monitoring following initiation of NIV, do not assume that he will fail because of his need for intubation in the past.

2. **"This child is in obvious respiratory distress. We need to start BiPAP at maximal settings to address his distress promptly."**
Initiation of BiPAP in pediatric patients can be challenging. Young children may be frightened by the full-face mask and high gas flow. It is important to allow children to become familiar with the mask and airflow. This requires coaching and reassurance on the part of the respiratory therapist and physician. It is best to start with lower IPAP and EPAP settings and gradually increase settings over time rather than start immediately with high-pressure settings. Anxiety alone may contribute to early BiPAP failure.

3. **"This child has severe asthma, and I think he would benefit from a trial of BiPAP, but he is claustrophobic, and I am worried that the oronasal mask may cause anxiety."**
It is important to take the time to provide reassurance to the anxious child. Many children require coaching and a little time to become familiar with the mask and high gas flow. As above, starting treatment with lower IPAP and EPAP settings with gradual titration may improve the child's tolerance of the positive airway pressure. In the claustrophobic child, other options include selection of a nasal mask. While the nasal mask may result in air leaking around the mouth of the mask, an anxious child may have better tolerance of this type of mask and still benefit from the positive pressure. Another option would be to provide a small amount of sedation with midazolam or ketamine. As a bronchodilator, ketamine has an added advantage in children with asthma.

4. **"This child recently underwent repair of a tracheoesophageal fistula. Intubation may be difficult, so we should apply nasal CPAP instead."**
Positive airway pressure is contraindicated after recent upper airway and upper gastrointestinal surgery. Respiratory support options should be carefully considered in this patient population, and the pediatric surgery team should be notified as soon as possible when these children present with respiratory distress.

5. **"We are short-staffed today, and intubating this patient would require a dedicated respiratory therapist. Let's try BiPAP instead."**
A common misconception is that NIV will require fewer resources than invasive ventilation. NIV is complex and can be labor-intensive. It requires experienced nurses and respiratory therapists, and patients must be monitored very closely, especially during the first hour after initiation of therapy. NIV may not be suitable for an understaffed ED.

6. **"This infant is on 2 L/min of humidified high-flow nasal cannula but does not appear to be improving. I would like to increase the airflow, but I am worried that this may irritate his nasal passages."**
Because the gas in the HHFNC system is nearly 100% humidified and warmed, infants tolerate higher airflows up to 8 L/min. Whereas high airflow with traditional nasal cannula can cause irritation and dryness of the nasal mucosa, the warmed humidified oxygen provided in the HHFNC system generally prevents this side effect and is well tolerated.

is tachypneic, you decrease your I time slightly to 0.4. An oronasal mask is used to minimize air leak and ensure an appropriate mask fit. The patient is monitored closely and settings are gradually increased to an IPAP of 12 cm H_2O and an EPAP of 6 cm H_2O. Your patient appears more comfortable with decreased retractions at these settings. His respiratory rate falls from 28 breaths/min to 18 breaths/min. You ask your nurse and respiratory therapist to remain in the room with the patient and to repeat vital signs every five minutes for the next 30 minutes while you contact your critical care colleagues and prepare for transport to the pediatric intensive care unit.

The Vapotherm Recall

This paragraph is included for informational purposes only. It is not meant to endorse any product or manufacturer.

Vapotherm, Inc., of Stevensville, Maryland, issued a nationwide recall of all Vapotherm 2000i high-flow humidification devices in December 2005 due to concerns of a possible association between this device and positive Ralstonia species cultures.[93] Ralstonia species are gram-negative bacilli that grow well in warm, moist environments. Ralstonia have generally exhibited low virulence in humans, and they are an infrequent cause of infection in immunocompetent patients.[94] However, they have been implicated in several prior nosocomial outbreaks involving contaminated water sources.[95-97] In the months preceding the recall, Ralstonia was cultured from clinical specimens and from the water side of the filter cartridges used in several Vapotherm 2000i devices.[93] In response to these concerns, Vapotherm, Inc., issued a voluntary recall of the device and developed a new disinfection protocol to include the use of high-level disinfectants as well as sterile water in the water chamber instead of tap water. The company recommends disinfection of the Vapotherm unit between patients or after 30 days of use in a single patient. The new protocol also recommends replacement of the filter cartridge between patients and after 30 days of use.[94] Following an investigation by the CDC and approval by the Food and Drug Administration (FDA), Vapotherm 2000i was re-introduced to the market in January 2007. Vapotherm, Inc., subsequently introduced a new high-flow oxygen-delivery device, Precision Flow™, in December 2007. This new device has a completely disposable patient circuit, as well as a vapor transfer cartridge, which prevents contact between the water source and the breathing gas. To date, there have been no infection concerns with the Precision Flow™ device.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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CME Questions

1. **Risks of intubation include which of the following:**
   a. Upper airway trauma
   b. Misplacement of the endotracheal tube
   c. Aspiration
   d. Barotrauma/pneumothorax
   e. All of the above

2. **Potential advantages of noninvasive ventilation over endotracheal intubation include all of the following EXCEPT:**
   a. Decreased risk of upper airway trauma
   b. Decreased risk of subglottic stenosis
   c. Decreased risk of gastric insufflation
   d. Decreased risk of ventilator-associated pneumonia

3. **Noninvasive ventilation includes which of the following techniques?**
   a. External negative pressure ventilation
   b. Continuous positive airway pressure
   c. Bi-level positive airway pressure
   d. All of the above

4. **Noninvasive positive pressure ventilation provides respiratory support through all of the mechanisms listed below EXCEPT:**
   a. Decreases work of breathing by unloading the diaphragm and accessory muscles
   b. Decreases functional residual capacity
   c. Improves upper airway patency

5. **Which of the following is a contraindication to the use of noninvasive ventilation?**
   a. Diarrhea
   b. Nasal congestion
   c. Tachypnea
   d. Impaired mental status

6. **Bi-level positive airway pressure:**
   a. Cycles between a peak inspiratory airway pressure and a peak expiratory airway pressure
   b. May decrease cardiac output in children with poor cardiac function
   c. May be delivered via a specific bi-level positive pressure device or via a traditional ventilator set to bi-level pressure support settings
   d. All of the above

7. **You decided to place a 28-day-old infant with bronchiolitis on nasal CPAP. Which of the following is the preferred external interface for this patient?**
   a. Single-nasal prong
   b. Nose mask
   c. Full-face mask or oronasal mask
   d. Short, wide bi-nasal prongs

8. **All of the following are advantages of humidified high-flow nasal cannula EXCEPT:**
   a. The HHFNC system delivers cooled, humidified air via nasal cannula.
   b. Flow rates up to 8 L/min can be achieved in infants.
   c. Flow rates up to 40 L/min can be achieved in adolescents and adults.
   d. HHFNC provides airway distending pressure which may help stabilize the highly pliable chest wall in young infants.

9. A 12-year-old male with asthma presents to the pediatric emergency department with diffuse inspiratory and expiratory wheezing, increased work of breathing, and tachypnea. He has little improvement following initiation of continuous albuterol nebulization, intravenous magnesium, and intravenous methylprednisolone. You decide to initiate therapy with BiPAP. All of the following are signs of a positive response to treatment EXCEPT:
   a. Decreased accessory muscle use
   b. Improved oxygenation
   c. Decreased respiratory rate
   d. Hypotension

10. Following initiation of BiPAP, your patient is having difficulty tolerating the oronasal mask. Before terminating the trial, you should do all of the following EXCEPT:
   a. Ensure that the mask size is appropriate for the patient.
   b. Start with maximal IPAP and EPAP pressure settings to ensure adequate gas flow.
   c. Consider sedation with midazolam.
   d. Consider sedation with ketamine.

11. Which of the following is an advantage of noninvasive ventilation when compared to endotracheal intubation?
   a. The patient requires minimal monitoring with NIV.
   b. The patient can communicate with health care providers with NIV.
   c. The patient requires more sedation with NIV.

12. In which of the following situations should an emergency care provider switch from noninvasive ventilation to endotracheal intubation?
   a. The patient has worsening agitation.
   b. The patient has worsening hypoxia.
   c. The patient has worsening respiratory distress.
   d. When any of the above occur.

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EVIDENCE-BASED PRACTICE RECOMMENDATIONS

Noninvasive Ventilation Techniques In The Emergency Department: Applications In Pediatric Patients

Deis J, Abramo T. June 2009; Volume 6 Number 6

This issue of *Pediatric Emergency Medicine Practice* reviews the history of noninvasive ventilation, the rationale for its use, and the evidence supporting its use in children with acute and chronic respiratory failure. For a more detailed and systematic look at the latest evidence on pediatric NIV as well as additional information such as clinical pathways and other information not noted here, see the full text article at www.ebmedicine.net.

Key Points	Comments
NIV avoids many of the risks associated with invasive ventilation, including upper airway trauma, subglottic stenosis, vocal cord dysfunction, and nosocomial infections.[2,3*]	In children with asthma, intubation carries a higher risk for complications including pneumothoraces and pneumomediastinum.[35-38]
Patients receiving NIV require less sedation than patients receiving mechanical ventilation. Children do not require paralysis, and when sedation is required, small doses of benzodiazepines are usually sufficient.[35,37-39,51]	Additional advantages of NIV include the patient's ability to communication with health care providers, decreased risk of airway trauma, decreased cost, and a potentially decreased length of hospital stay.[37-39]
Recognize the contraindications to NIV. Patients with hemodynamic instability, excessive secretions, upper gastrointestinal bleeding, altered mental status, or recent upper airway or GI surgery should not receive NIV.[31]	Respiratory support options should be carefully considered in patients with recent upper airway and upper gastrointestinal surgery, and the pediatric surgery team should be notified as soon as possible when these children present with respiratory distress.[31]
Before initiating therapy with BiPAP or CPAP, ensure that the patient is on a full cardiorespiratory monitor with continuous pulse oximetry and that there is an experienced nurse and/or respiratory therapist available to monitor the patient.	NIV is contraindicated if there is inadequate staff to monitor the patient.
When initiating treatment with BiPAP or CPAP in children, provide the patient with the opportunity to become familiar with the mask and airflow. Children who receive reassurance and coaching prior to therapy are more likely to succeed.[51,56]	In the claustrophobic child, consider a nasal mask. While the nasal mask may result in air leaking around the mouth of the mask, an anxious child may have better tolerance of this type of mask and still benefit from the positive pressure. Alternatively, consider providing a small amount of sedation with midazolam or ketamine.[51]
When initiating BiPAP or CPAP, start with low pressure settings and increase the pressure support gradually over time to avoid patient discomfort and early failure of the technique.[56]	Gradual titration may improve the child's tolerance of the positive airway pressure. Anxiety alone may contribute to early BiPAP failure.
Carefully monitor children during the first hour after initiation of NIV. Signs of positive response to treatment include decreased respiratory rate, decreased retractions and accessory muscle use, reduced airway occlusion events, improved oxygenation on pulse oximetry and blood gases, and improved lung volumes on chest radiographs.[31,51,61]	Intubate patients with worsening respiratory distress, increasing lethargy, or hemodynamic instability.
While pressures as high as 15 cm H_2O can be achieved with CPAP, pressures above 15 cm H_2O are rarely needed. The typical range is 5 to 10 cm H_2O.[40,41]	CPAP can be delivered through oronasal masks, nose masks, nasopharyngeal prongs, single-nasal prongs, and short bi-nasal prongs. Short bi-nasal prongs are the preferred method for neonates and infants.[40]
For Bi-PAP, the typical setting is 10 to 16 cm H_2O for IPAP and 5 to 10 cm H_2O for EPAP.[51]	Aerosols, such as albuterol and nebulized epinephrine, may be delivered through the new BiPAP devices.

* See reverse side for reference citations.

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