Transcatheter coronary infusion of supersaturated oxygen therapy in acute myocardial infarction

Clinical Policy ID: CCP.1499

Recent review date: 10/2025

Next review date: 2/2027

Policy contains: Acute myocardial infarction; aqueous oxygen therapy; hyperoxemic reperfusion therapy; percutaneous coronary intervention; STEMI; ST-segment elevated myocardial infarction; supersaturated oxygen.

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Coverage policy

Intracoronary supersaturated oxygen therapy (otherwise known as aqueous oxygen therapy, hyperoxemic reperfusion therapy, or super-oxygenation therapy) is investigational/not clinically proven and, therefore, not medically necessary for the treatment of reperfusion during acute myocardial infarction.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Percutaneous coronary intervention.
- Percutaneous transluminal coronary angioplasty with or without atherectomy and/or stent placement.

Background

Following an acute myocardial infarction, early restoration of blood flow through the blocked coronary artery with the use of thrombolytic therapy or primary percutaneous coronary intervention is the most effective approach to reduce the size of a myocardial injury and improve clinical outcomes. Although early reperfusion therapy in ST-elevation myocardial infarction has reduced mortality overall in the past several decades, reperfusion after ischemia may contribute to additional cell death and increases in infarct size. This, known as myocardial reperfusion injury, culminates in the death of cardiac muscle cells that were viable immediately before reperfusion (Kloner, 2021). It may partly explain why, despite optimal reperfusion to the heart, the mortality after an acute myocardial infarction approaches 12% (Jenca, 2021), and the incidence of cardiac failure after one is almost 25% in Medicare-eligible patients (Krumholz, 2019).

Chen (2021) also noted that despite high rates of epicardial coronary flow restoration to the infarct-related artery, heart muscle salvage is often suboptimal even with sustained patency. This issue has been attributed to late reperfusion, microvascular dysfunction or lack of reflow, reperfusion injury, and other mechanisms which may progress over hours to days.

Noninvasive imaging methods, such as cardiac magnetic resonance imaging and technetium-99m sestamibi single photon emission computed tomography, provide important insights regarding the prognosis of patients who experience problems at the extreme end of the spectrum, such as myocardial regions with no reflow, hemorrhage, and pathologies within the infarcted necrotic core (Spears, 2019). For example, infarct size measured by cardiac magnetic resonance imaging or technetium-99m sestamibi single photon emission computed tomography within one month after primary percutaneous coronary intervention was a strong prognostic indicator of all-cause mortality and heart failure hospitalization within one year (Stone, 2016).

Therapies to further reduce infarct size after timely epicardial reperfusion have been studied over several decades, but many have failed to produce a benefit in clinical trials. Intracoronary supersaturated oxygen therapy is an emerging adjunct to percutaneous coronary intervention for patients with anterior acute myocardial infarction. Intracoronary supersaturated oxygen therapy delivers a super-oxygenated saline solution with the patient's arterial blood to targeted ischemic myocardial regions, thereby increasing oxygen diffusion to the ischemic area, restoring microvascular flow, and protecting the myocardium from further injury (Kloner, 2021).

In 2019, the U.S. Food and Drug Administration granted premarket approval to the TherOx Downstream® System (TherOx Inc., Irvine, California). TherOx is indicated for "the preparation and delivery of SuperSaturated Oxygen Therapy to targeted ischemic regions perfused by the patient's left anterior descending coronary artery immediately following revascularization by means of percutaneous coronary intervention with stenting that has been completed within six hours after the onset of anterior acute myocardial infarction symptoms caused by a left anterior descending artery infarct lesion" (U.S. Food and Drug Administration, 2019).

Findings

Across guidelines, systematic evaluations, and clinical studies, transcatheter coronary infusion of supersaturated oxygen therapy shows the clearest signal of benefit when delivered after percutaneous coronary intervention for large anterior infarction within six hours of symptom onset. Trials demonstrate reductions in infarct size and improved myocardial recovery under these conditions, while early safety outcomes are generally comparable to standard care, aside from access-site bleeding that has improved with lower-profile devices. However, effects

on long-term survival and major adverse cardiovascular events remain inconsistent, with small samples and heterogeneity limiting certainty (O'Neill, 2007; Stone, 2009; David, 2019; Hanson, 2015; Chen, 2021; Lawton, 2021; Zhang, 2024).

Guidelines

The 2021 American College of Cardiology and American Heart Association guideline for coronary artery revascularization does not address intracoronary supersaturated oxygen therapy (Lawton, 2021). The 2025 American College of Cardiology, American Heart Association, American College of Emergency Physicians, National Association of Emergency Medical Services Physicians, and Society for Cardiovascular Angiography and Interventions guideline for acute coronary syndromes emphasizes primary percutaneous coronary intervention as the reperfusion strategy of choice. It provides no class recommendation for intracoronary supersaturated oxygen infusion, and stresses instead that routine supplemental oxygen in non-hypoxic patients confers no cardiovascular benefit (Rao, 2025).

A 2024 Society for Cardiovascular Angiography and Interventions best-practice statement notes that the therapy received United States Food and Drug Administration approval in 2019 for reduction of infarct size in patients with anterior infarction reperfused within 6 hours. It describes device refinements that lowered bleeding risk and reports an average infarct-size reduction of about 28% in pivotal studies, while highlighting the need for continued surveillance (Tamis-Holland, 2024).

Systematic reviews

A 2025 systematic review and meta-analysis of 4 studies (N = 1,610) found that adding intracoronary supersaturated oxygen after percutaneous coronary intervention reduced the amount of heart muscle damaged by about 4 percentage points compared with percutaneous coronary intervention alone, with little variation between studies. Across the same evidence set, there was no signal of increased early harm, as rates of major adverse cardiovascular events, death, reinfarction, and repeat revascularization were similar between groups. The review combined 2 randomized trials and 2 prospective cohorts, judging the randomized trials at low risk of bias and the observational cohorts at moderate risk. Overall, the findings support consistent infarct-size reduction but highlight the need for larger trials to determine whether these imaging benefits translate into fewer complications (Aghna, 2025).

Meta-analyses

Randomized evidence consistently shows that when therapy is delivered within 6 hours in large anterior infarction, infarct size is smaller compared with control, while early composite adverse events and 30-day mortality do not differ significantly (O'Neill, 2007; Stone, 2009). Access-site bleeding observed with earlier delivery systems lessened after lower-profile catheters were introduced (Stone, 2009).

Other evidence

Single-arm and feasibility studies demonstrate technical practicality and favorable safety profiles. A 100-patient trial achieved 98% delivery success and reported a 30-day composite adverse event rate of 7.1%, with median infarct size declining from 24.1% at 4 days to 19.4% at 30 days (David, 2019). One-year follow-up found lower rates of death and new-onset heart failure or hospitalization compared with controls, though reinfarction and stent thrombosis were similar (Chen, 2021). Earlier pivotal work showed no overall infarct-size reduction but post hoc analyses suggested benefits for anterior infarction treated within 6 hours, including smaller infarct size, greater improvement in wall motion, and better ST-segment resolution (O'Neill, 2007). A subsequent trial restricted to this subgroup prospectively confirmed smaller infarct size with non-inferior safety (Stone, 2009). A

pilot feasibility study also established the technical basis for this therapy (Hanson, 2015). Longer-term outcomes and broader generalizability remain uncertain.

In 2025, we reorganized the findings section to integrate new guideline statements (Rao, 2025), a best-practice consensus (Tamis-Holland, 2024), and a systematic review (Aghna, 2025). No policy changes were warranted.

References

On September 10, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were super oxygenated, supersaturated oxygen, oxygen delivery, percutaneous coronary intervention, angioplasty, reperfusion, and acute myocardial infarction. We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

10/2021: initial review date and clinical policy effective date: 11/2021

10/2022: Policy references updated.

10/2023: Policy references updated.
10/2024: Policy references updated.
10/2025: Policy references updated.