REVIEW ARTICLE

Oxygen Therapy Confers Little Benefit in Patients with Acute ST-Segment Elevation Myocardial Infarction: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective • We aimed to investigate the clinical benefit of oxygen therapy in patients with acute ST-segment elevation myocardial infarction (STEMI).

Methods • We searched PubMed, Embase and the Cochrane Library from database inception to June 2020 to identify randomized controlled trials (RCTs) on oxygen therapy in acute STEMI. Literature screening, data extraction and study quality assessment were independently carried out by the 2 investigators according to the predefined eligibility criteria, and RevMan 5.3 analysis software was utilized for all analyses.

Results • Finally, 5 RCTs with a total of 4824 patients with STEMI were eligible for further meta-analysis. The RCT results demonstrated that oxygen therapy exerted non-significant effects in reducing the risks for short-term all-cause mortality (risk ratio [RR] = 1.21; 95% CI, 0.80-1.53; P = .53), cardiac arrest (RR = 1.20; 95% CI, 0.94-1.54; P = .79), recurrent myocardial infarction (MI) (RR = 0.68; 95% CI, 0.43-1.08; P = .10) and cardiogenic shock (RR = 0.81; 95% CI, 0.58-1.15; P = .24) and the incidence of other outcome indicators of acute STEMI.

Conclusions • Oxygen therapy does not provide more benefits than adverse effects in patients with acute STEMI. Personalized oxygen treatment based on dynamic oxygen saturation is recommended in patients with hypoxia. Supplemental oxygen in patients with acute STEMI has no effect on reducing infarct size, and has no benefit in all-cause mortality, cardiogenic shock, etc. (*Altern Ther Health Med.* 2023;29(2):282-288)

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INTRODUCTION

Acute myocardial infarction (AMI) is myocardial necrosis caused by acute or persistent myocardial ischemia and hypoxia after acute obstruction of a coronary artery. It features dramatic onset, rapid progression, high mortality rates and permanent disability. It only allows emergency rescue within a narrow timeframe, notwithstanding the fact that advances in monitoring and reperfusion therapy have recently aided in the decline in mortality in patients with AMI. Acute ST-segment elevation myocardial infarction (STEMI) is the most common type of AMI.

Inhaled oxygen was first used in patients suspected of AMI approximately a century ago and subsequently applied from one type of cardiovascular disease to another. STEMI remains a significant contributor to morbidity and mortality worldwide.[1] To date, supplemental oxygen as a routine treatment for acute STEMI has been officially recommended in several management guidelines.[2] Although several studies have ascertained that inhaled oxygen, especially in high concentrations, can treat myocardial injury in patients with STEMI, most are clinical studies without randomization, concealment and blinding or animal experiments, which merely provide not-so-strong evidence about the effectiveness of oxygen therapy. Based on recent new evidence, routine oxygen therapy is no longer recommended in patients with myocardial infarction (MI) without hypoxemia.

Recently, more studies have yielded inconsistent results. It was reported that high concentrations of oxygen may exacerbate myocardial injury during coronary artery contraction due to the oxidative stress response. Other negative cardiovascular effects after oxygen supplementation in patients with AMI include

increases in blood pressure, systemic vascular resistance and infarct size. There is also evidence that oxygen supplementation as a routine treatment in patients with acute STEMI with normal oxygen saturation only provides negligible improvement in 1-year all-cause mortality. Supplemental oxygen exposure in the first 12 h after STEMI was associated with a clinically significant increase in cTnI and CK release.[3] The DETermination of the role of Oxygen in suspected Acute Myocardial Infarction (DETO2X-AMI) trial did not find any benefit of oxygen therapy compared with ambient air in normoxemic patients with suspected acute MI.[4] The location of the culprit vessel probably has no effect on the role of supplemental oxygen therapy in patients with STEMI.[5] Even so, the vast majority of patients with STEMI, including many patients without hypoxemia, still routinely undergo oxygen therapy as part of their daily care. Several surveys on the attitude of medical professionals to oxygen therapy found that approximately half of responders believe that oxygen therapy is capable of reducing mortality and relieving chest pain, and most were of the opinion that it at least caused no harm.

Despite the proven disadvantages of conventional oxygen therapy in patients with AMI with normal oxygen saturation levels, new findings cast increasing doubt on whether early oxygen intervention should be used in patients with acute STEMI, and there is growing evidence that hyperoxia therapy may have adverse effects in these patients.[6-13] Some studies ascertained that the efficacy of early oxygen therapy in acute STEMI remained uncertain and might even increase the risk for recurrent MI and prolong the average length of hospital stay.[12-16] Therefore, we performed a meta-analysis of randomized controlled trials (RCTs) to provide stronger evidence as to whether oxygen therapy conveys benefits in patients with acute STEMI. Our study will provide a reference for a more reasonable and flexible strategy in acute STEMI management.

MATERIALS AND METHODS

Literature Search Strategy

We searched RCTs of oxygen therapy in acute STEMI published in PubMed, Embase, and the Cochrane Library from their inception to June 2020. The combination of subject headings and free text words were utilized for the following concepts: myocardial infarction, oxygen inhalation therapy, randomized controlled trials and human trials. Only English-language studies were searched. The specific retrieval strategy is shown in the supplementary materials.

Inclusion and exclusion criteria

Inclusion criteria. Studies were included if: (1) they were RCTs; (2) patients were confirmed with acute STEMI; (3) normal-pressure oxygen therapy was delivered at hospitals in the treatment group and medical air or titrated oxygen in the control group; (4) at least one of the following outcome indicators was utilized: short-term all-cause mortality or the recurrence rates of cardiogenic shock, myocardial ischemia, or MI. We selected RCTs that included patients with normal oxygen saturation.

Exclusion criteria. Articles were excluded if: (1) they failed to provide comprehensive data that could be extracted; (2) they were conferences, reviews, expert opinions, non-open access articles or duplicates; (3) non-acute STEMI was being studied; (4) studies were without controlled comparisons, or had questionable design or were of poor quality.

Literature screening

The literature review and data extraction were performed by the 2 investigators independently. Any disagreement was discussed with a third researcher. During the initial screening, we removed duplicate articles after reading titles and abstracts. In the next stage, we read the full texts of the remaining articles to determine whether they fulfilled the inclusion criteria. Finally, the name of the first author, publication year, country, sample size, age, gender, follow-up duration, interventions and outcome indicators were extracted from the articles included in the meta-analysis.

Literature quality evaluation

The risk of bias in the RCTs included was evaluated using the Cochrane Handbook version 5.3.0 from 6 domains: random sequence generation and allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias. Each item in the handbook was assigned a low, high, or unclear risk of bias for evaluation. Studies that completely and partially met the inclusion criteria were rated Grade A and B, respectively, suggesting the smallest and moderate likelihood of bias; those not completely satisfying the criteria indicated a high possibility of bias and were rated Grade C. Quality assessment was performed by the 2 researchers independently. Any disagreement was resolved by consensus or by consultation with the third researcher.

Statistical Analysis

All meta-analyses of RCTs were performed using RevMan 5.3.0 statistical software provided by the Cochrane Collaboration. Effect sizes for dependent measures were expressed as standardized mean differences (SMDs) with 95% CIs; those for enumeration data were expressed as relative risk (RR) with 95% CIs. Heterogeneity between studies was tested using the chi-square test and indicated by a $P \leq .1$ and an $I^2 \geq 50\%$ and a random-effect model was used for meta-analysis. If homogeneity between studies was observed ($P > .1$; $I^2 < 50\%$), a fixed-effect model was used. The statistical significance level was set at $P < .05$.

RESULTS

Literature Search

In the first stage, 1956 relevant studies were retrieved, including 576 from PubMed, 412 from Embase and 759 from the Cochrane Library. After eliminating duplicates by using EndNote Click software and reading titles, 1446 studies were initially selected. In the second stage, 31 studies were selected

after the title and abstract review, 21 of which were full-text articles. Based on the full-text reading, 10 studies satisfied the inclusion criteria. After removing 5 that were low quality, 5 RCTs that completely met the eligibility criteria were ultimately included in the meta-analysis. The sample size was 9728 patients with acute STEMI, including 4824 receiving oxygen therapy and 4905 inhaling medical air (the control group). The literature screening process and results are shown in Figure 1 and the basic characteristics of the RCTs included in the study are summarized in Tables 1 and 2.

Quality of RCTs

All 5 RCTs were rated high-quality. Specifically, random sequence generation was carried out in each study, and 4 studies[17-20] described the specific procedures using a computer and 1 mentioned the use of a random number table. In addition, 2 studies[17,18] elaborated on the procedures of allocation concealment using the sealed envelope system, and none of the others did. All 5 studies failed to provide a clear description of blinding. In terms of incomplete outcome data, all the RCTs included reported the missing-data problem and the number of patients and provided specific reasons; 2 studies reported selective reporting of results.

META-ANALYSIS

All-cause mortality

The incidence of short-term (within 30 days including the in-hospital stay) mortality after oxygen therapy was reported in 2 RCTs, and a non-significant difference was observed between the oxygen therapy and control groups. Our meta-analysis showed that patients with acute STEMI did not benefit from oxygen therapy in short-term all-cause mortality decline vs the control group (RR = 1.21; 95% CI, 0.80-1.53; P =.53), as shown in Figure 1.

Figure 1. Flow diagram of literature screening.

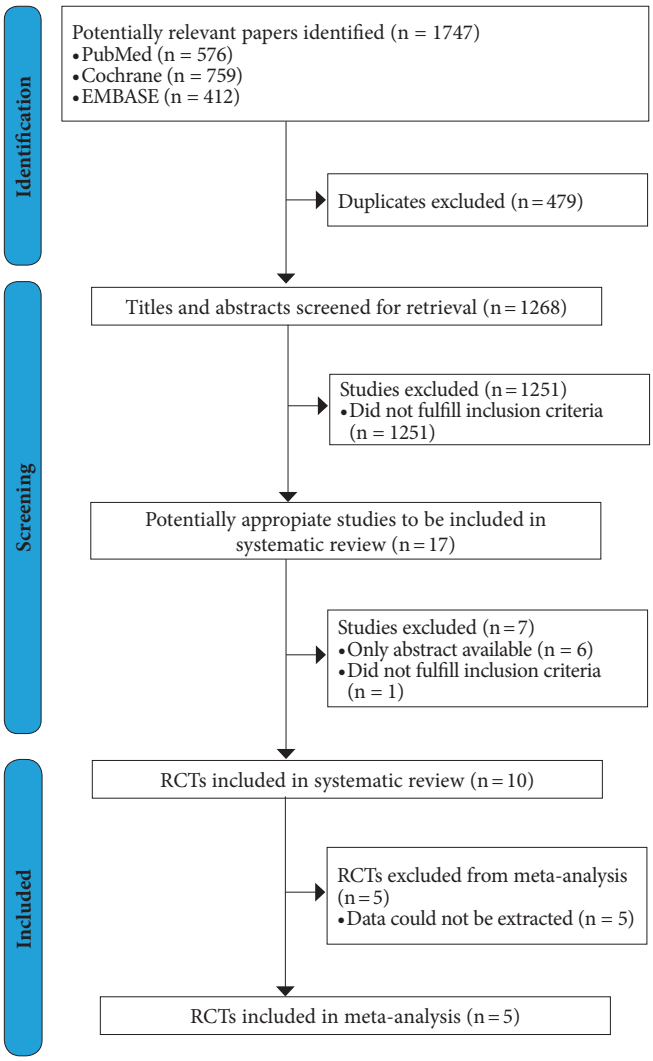


Table 1. Literature Information on the Effect of Oxygen Therapy in Patients with Acute ST-segment Elevation Myocardial Infarction

First author, publication year	Number of patients (O/C)	Country	Study design	Oxygen therapy Group (O)	Control group (C)	Outcome indicators	Follow-up duration
Hofmann, 2017	3311/3318	Sweden	Unblinded RCT	Mask oxygen (6 L/min) 6-12 h	Air	1,3,4	395 days
Hofmann, 2018	1361/1446	Sweden	Unblinded RCT	Mask oxygen (6 L/min) 6-12 h	Air	1,2,3	1356 days
Khoshnood, 2016	46/49	Sweden	Unblinded RCT	Mask oxygen (10 L/min) 6-12 h	Air	1,2,3,4	After PCI
Khoshnood, 2017	46/41	Sweden	Unblinded RCT	Mask oxygen (10 L/min) 6-12 h	Air	1,2,3,4	6 months
Khoshnood, 2018	60/51	Sweden	Unblinded RCT	Mask oxygen (10 L/min) 6-12 h	Air	1,2,3,4	1-6 days

Note: Outcome indicators 1 = all-cause mortality; 2 = cardiac arrest; 3 = recurrent myocardial infarction; 4 = cardiogenic shock

Abbreviations: C, control group; O, oxygen group; PCI, percutaneous transluminal coronary intervention; RCT, randomized controlled trial.

Table 2. Literature Sources and Outcome Results of the Five Randomized Controlled Trials Included in the Study (N = 4824)

First author, publication yr	# of patients (O/C, patients)		All-cause mortality		Cardiac arrest		Recurrent myocardial infarction		Cardiogenic shock	
	Oxygen therapy group	Control group	Oxygen therapy group	Control group	Oxygen therapy group	Control group	Oxygen therapy group	Control group	Oxygen therapy group	Control group
Hofmann, 2017	3311	3318	53	44	79	63	17	34	32	37
Hofmann, 2018	1361	1446	26	29	56	51	12	11	25	33
Khoshnood, 2016	46	49	-	-	1	3	1	0	1	1
Khoshnood, 2017	46	41	-	-	-	-	-	-	0	1
Khoshnood, 2018	60	51	-	-	-	-	-	-	1	2

Figure 1. Forest plot of meta-analysis of the effect of oxygen therapy on all-cause mortality for acute ST-segment elevation myocardial infarction

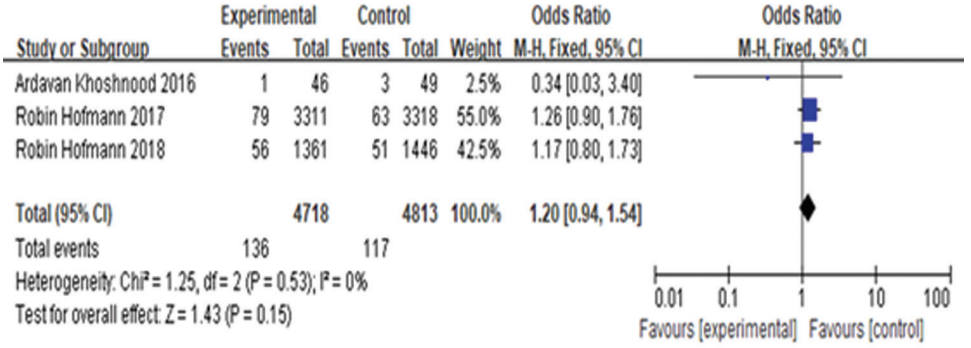


Figure 2. Forest plot of meta-analysis of the effect of oxygen therapy on cardiac arrest in acute ST-segment elevation myocardial infarction

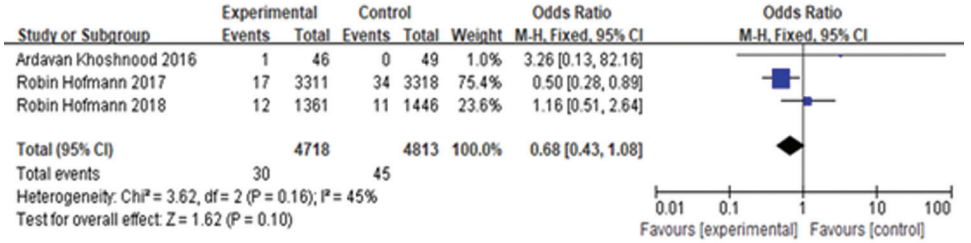
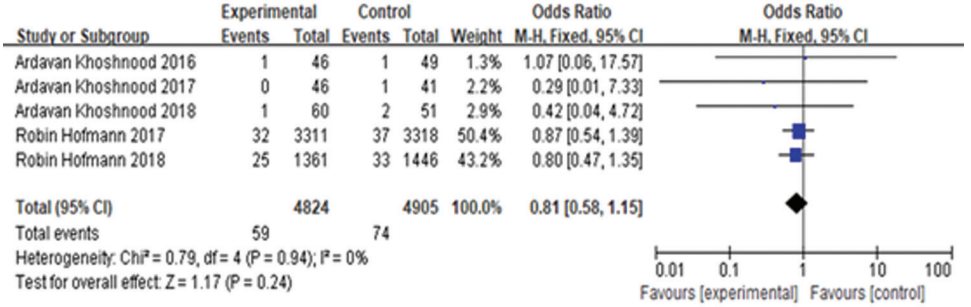


Figure 3. Forest plot of meta-analysis of the effect of oxygen therapy in the recurrence rate of myocardial infarction in acute ST-segment elevation myocardial infarction.



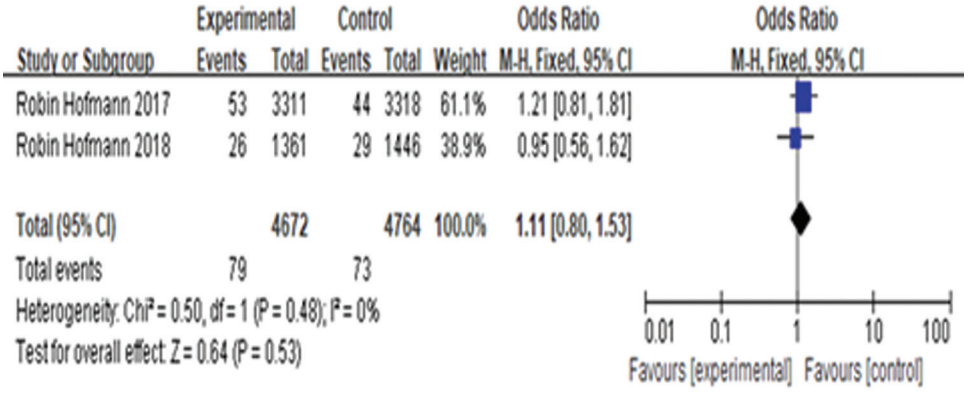
Incidence of cardiac arrest

A total of 3 studies reported the number of patients with cardiac arrest. The meta-analysis showed that there was a non-significant improvement in cardiac arrest after conventional oxygen therapy (RR = 1.20; 95% CI, 0.94-1.54; *P* = .15) (see Figure 2).

Recurrence rate of myocardial ischemia or infarction

A meta-analysis of 3 studies calculating the incidence of recurrent myocardial ischemia or infarction was performed. Oxygen therapy was not found to be beneficial in lowering the recurrence of myocardial ischemia or infarction vs the control groups (RR = 0.68; 95% CI, 0.43-1.08; *P* = .10) (see Figure 3).

Figure 4. Forest plot of meta-analysis of the effect of oxygen therapy on the incidence of cardiogenic shock in patients with acute ST-segment elevation myocardial infarction.



Incidence of cardiogenic shock

All 5 studies analyzed the incidence of cardiogenic shock after oxygen therapy. However, there was a non-significant reduction in the incidence of cardiogenic shock after oxygen therapy vs the control groups in all of the RCTs (RR = 0.81; 95% CI, 0.58-1.15; $P = .24$) (see Figure 4).

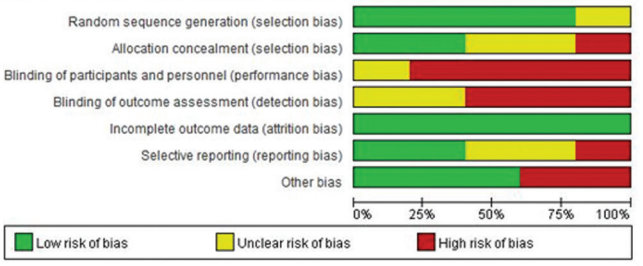
Other studies consistently reported the same results: patients suspected of acute STEMI without hypoxemia did not benefit from routine oxygen supplementation in reducing 1-year all-cause mortality.[21-22] Our meta-analysis demonstrated that oxygen therapy offered no reductions in the incidence of cardiac arrest (pooled RR = 1.20; 95% CI, 0.9-1.54; $P = .751$; $I^2 = 0.0\%$) (see Figure 2), the recurrence rate of myocardial ischemia or infarction (pooled RR = 0.68; 95% CI, 0.43-1.08; $P = .10$; $I^2 = 45\%$) (see Figure 3), and the occurrence of cardiogenic shock (pooled RR = 0.81; 95% CI, 0.58-1.15; $P = .24$; $I^2 = 0.0\%$) (see Figure 4) vs the control group. Therefore, there is no conclusive evidence from RCTs to support the benefit of routine oxygen therapy in patients with acute STEMI.[23]

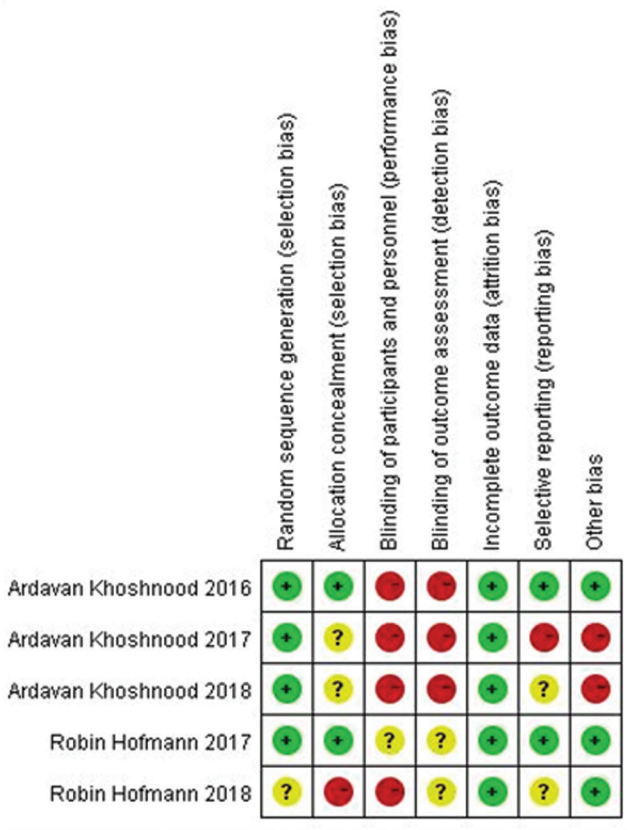
DISCUSSION

Our meta-analysis, which included 4824 patients from 5 RCTs, demonstrated that conventional oxygen therapy did not confer improvement in the short-term incidence of all-cause mortality, cardiac arrest, myocardial ischemia or infarction or cardiogenic shock in patients with acute STEMI without hypoxemia. This may be due to the nature of oxygen, which promotes leukocyte chemotaxis and inflammatory processes that may increase the possibility of cardiomyocyte death. In this process, reactive oxygen species may enhance myocardial depolarization via activation of the oxidative stress response, which can lead to tachycardia and even ventricular fibrillation or other fatal arrhythmias. The researchers found that in patients with acute stroke without hypoxemia, there was a non-significant difference in mortality between routine oxygen inhalation (2 to 3 L) vs medical air. Hyperoxia is associated with increased mortality after cardiac arrest.

The controversy about whether oxygen therapy is appropriate in patients with acute STEMI with normal

Figure 5. Risk-of-bias assessment of RCTs of oxygen therapy in acute ST-segment elevation myocardial infarction.





saturation has been going on for years. Early studies found that increased arterial oxygen content after oxygen inhalation might benefit the ischemic myocardium by providing a sufficient oxygen supply, thereby reducing infarct size. Our meta-analysis further confirmed that oxygen therapy conferred no benefit in patients with normal oxygen saturation.

Recently, public health officials in the United States, the United Kingdom and other European countries began to use caution with oxygen inhalation treatment and changed the criteria for oxygen therapy in AMI. According to the British Thoracic Society guidelines for emergency oxygen application, it is only approved for emergency use in patients with hypoxemia. Heart failure guidelines in Canada, Europe and the United States suggest that oxygen therapy can be indicated in patients with hypoxemia (especially arterial saturated oxygen [SaO_2] <90%, Class I: benefit > risk, level C confidence); in the absence of hypoxemia, conventional oxygen therapy is not recommended (Class III: risk > benefit, level C confidence). The 2004 American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guideline for the management of STEMI claims that oxygen therapy is indicated in patients with arterial oxygen saturation <90% (Class I), and oxygen supplementation is approved in all patients with AMI within the first 6 h (Class III). The 2013 ACC/AHA guideline for STEMI no longer recommends oxygen therapy but the use of oxygen supplementation based on oxygen saturation monitoring. In 2012, several European guidelines for the management of MI suggested the use of non-invasive blood oxygen monitoring for adequate oxygen supply. The upper limit for patients receiving oxygen therapy is <94%, as indicated by the 2015 European Society of Cardiology (ESC) guideline, and oxygen therapy is recommended in individuals with hypoxemia, considering its serious complications. Generally, authoritative guidelines state that oxygen therapy is suitable in patients with low oxygen saturation.

As for acute STEMI, our analysis provides stronger evidence that oxygen therapy conveys no benefit in normoxic patients, which conforms to the latest recommendation of the upper limit for oxygen therapy of 94% oxygen saturation. A *Cochrane review* showed that oxygen inhalation may increase mortality risk in patients with AMI vs air inhalation.[24] Compared with medical air, high-flow oxygen was not associated with a decrease in ischemic area, myocardial rescue or smaller infarct size before percutaneous transluminal coronary intervention.[25]

Although so far only a limited number of RCTs have provided evidence that oxygen inhalation has a non-significant effect in patients with MI worldwide, authoritative associations in the United States and European countries have raised awareness and have already taken action on problems with excessive oxygen therapy. The 2010 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiac Events claimed that only patients with acute coronary syndrome accompanied by hypoxia should receive titrated oxygen therapy before oxygen saturation reached 94%. The 2013 AFFC/AHA guidelines produced the altered recommendation in STEMI management that oxygen inhalation is only indicated in patients presenting with manifestations of hypoxia or shock.[26] The 2012 ESC Guidelines for the Treatment of STEMI also pointed out that non-invasive oxygen saturation monitoring should be used to avoid either hypoxemia or oxygen inhalation-induced hyperoxemia.[27]

Study Limitations

This study had the following limitations that may affect the credibility of our analysis. Only 5 RCTs were finally included, so the publication bias analysis that requires at least 10 studies was not available. In addition, significant heterogeneity in both oxygen flow rate and concentration was observed between studies, and the effect of each specific oxygen concentration on the patients could not be meta-analyzed due to the limited number of studies. Only 2 of the included RCTs conducted long-term follow-up, leaving the remaining studies with either a short-term or no follow-up for exploration of the post-treatment effects of oxygen therapy. Therefore, the insufficient follow-up data did not support a meta-analysis of the long-term efficacy of oxygen therapy, resulting in a bias. Of note, hypoxic patients were excluded from the RCTs, so the results are only applicable to normoxic patients, increasing the possibility of bias. Oxygen therapy in normoxic patients with STEMI should therefore be omitted.[28] Oxygen has no significant analgesic effect on chest pain in patients with STEMI,[19] and does not reduce the risk for all-cause mortality, recurrent ischemia or MI, heart failure or arrhythmias.[29]

CONCLUSIONS

Overall, our meta-analysis ascertains that patients with acute STEMI with normal oxygen saturation do not benefit from conventional oxygen therapy; there is no amelioration in all-cause mortality or declines in the incidence of recurrent MI, cardiac arrest or cardiogenic shock, which are consistent with previous studies of STEMI. Excessive oxygen therapy may even bring potential risks, notwithstanding unnecessary medical waste. Whether patients with acute STEMI are suitable for oxygen inhalation depends on their oxygen saturation and other indicators.

In future clinical studies, we need to pay more attention to thorough evaluation of a lower oxygen flow rate in particular patients with different SaO_2 ranges, with blood oxygen concentration tested and monitored by SaO_2.[30] Perhaps we should once again think about oxygen therapy in terms of its indication, contraindications, dose, route of administration and monitoring for outcomes and toxicity, just as with any other pharmaceutical intervention.[31] Avoiding routine oxygen therapy in patients with suspected or confirmed MI without hypoxemia at baseline saves significant expenditure for the health care system both with regards to medical and human resources.[32]

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CONFLICT OF INTEREST

None.

REFERENCES

1. Choudhury T, West NE, El-Omar M. ST elevation myocardial infarction. *Clin Med (Lond)*. 2016;16(3):277-282. doi:10.7861/clinmedicine.16-3-277
2. Kones R. Oxygen therapy for acute myocardial infarction-then and now. A century of uncertainty. *Am J Med*. 2011;124(11):1000-1005. doi:10.1016/j.amjmed.2011.04.034
3. Nehme Z, Stub D, Bernard S, et al; AVOID Investigators. Effect of supplemental oxygen exposure on myocardial injury in ST-elevation myocardial infarction. *Heart*. 2016;102(6):444-451. doi:10.1136/heartjnl-2015-308636
4. Andell P, James S, Östlund O, et al. Oxygen therapy in suspected acute myocardial infarction and concurrent normoxemic chronic obstructive pulmonary disease: a prespecified subgroup analysis from the DETO2X-AMI trial. *Eur Heart J Acute Cardiovasc Care*. 2020;9(8):984-992. doi:10.1177/2048872619848978
5. Mokhtari A, Akbarzadeh M, Sparv D, et al. Oxygen therapy in patients with ST elevation myocardial infarction based on the culprit vessel: results from the randomized controlled SOCCER trial. *BMC Emerg Med*. 2020;20(1):12. doi:10.1186/s12873-020-00309-y
6. Abuzaid A, Fabrizio C, Felpel K, et al. Oxygen therapy in patients with acute myocardial infarction: A systemic review and meta-analysis. *Am J Med*. 2018;131(6):693-701. doi:10.1016/j.amjmed.2017.12.027
7. Cabello JB, Burls A, Emparanza JI, Bayliss SE, Quinn T. Oxygen therapy for acute myocardial infarction. *Cochrane Database Syst Rev*. 2016;12(12):CD007160. doi:10.1002/14651858
8. Fu S, Lv X, Fang Q, Liu Z. Oxygen therapy for acute myocardial infarction: A systematic review and meta-analysis. *Int J Nurs Stud*. 2017;74:8-14. doi:10.1016/j.ijnurstu.2017.04.005
9. Hu X, Cheng S, Yin Y, Ning L, Xiang L, Zhou Y. The role of oxygen therapy in normoxemic acute coronary syndrome: A systematic review of randomized controlled trials. *J Cardiovasc Nurs*. 2018;33(6):559-567. doi:10.1097/JCN.0000000000000503
10. Khan AR, Abdulhak AB, Luni FK, et al. Oxygen administration does not influence the prognosis of acute myocardial infarction: A meta-analysis. *Am J Ther*. 2019;26(1):e151-e160. doi:10.1097/MJT.0000000000000475
11. Li SC, Zhang SS, Li ZF. Efficacy and safety of early oxygen therapy for acute myocardial infarction: A meta-analysis. *Chinese J Evidence-Based Med*. 2016;16(3):304-310.
12. Li WF, Huang YQ, Feng YQ. Oxygen therapy for patients with acute myocardial infarction: a meta-analysis of randomized controlled clinical trials. *Coron Artery Dis*. 2018;29(8):652-656.
13. Loomba RS, Nijhawan K, Aggarwal S, Arora RR. Oxygen in the setting of acute myocardial infarction: Is it really a breath of fresh air? *J Cardiovasc Pharmacol Ther*. 2016;21(2):143-149. doi:10.1177/1074248415598004
14. More harm than good in acute MI? Systematic review. *Euro Heart J*. 2009;30:617.
15. Søgaard P, Klausen IC, Rungby J, Faergeman O, Thygesen K. Lipoprotein(a) and oxygen-free radicals in survivors of acute myocardial infarction: effects of captopril. *Cardiology*. 1996;87(1):18-22. doi:10.1159/000177054
16. Zhang R, Zhu Y, Zhang M, Yin H, Wei J. Oxygen therapy versus conservative therapy in suspected uncomplicated myocardial infarction without hypoxemia: A meta-analysis of randomized controlled studies. *Hong Kong J Emer Med*. 2019;28(6):367-378, S1-S19.
17. Hofmann R, James SK, Jernberg T, et al.; DETO2X–SWEDEHEART Investigators. Oxygen therapy in suspected acute myocardial infarction. *N Engl J Med*. 2017;377(13):1240-1249. doi:10.1056/NEJMoa1706222
18. Hofmann R, Witt N, Lagerqvist B, et al.; DETO2X-SWEDEHEART Investigators. Oxygen therapy in ST-elevation myocardial infarction. *Eur Heart J*. 2018;39(29):2730-2739. doi:10.1093/eurheartj/ehy326
19. Khoshnood A, Akbarzadeh M, Carlsson M, et al. Effect of oxygen therapy on chest pain in patients with ST elevation myocardial infarction: results from the randomized SOCCER trial. *Scand Cardiovasc J*. 2018;52(2):69-73. doi:10.1080/14017431.2018.1439183
20. Khoshnood A, Akbarzadeh M, Roijer A, et al. Effects of oxygen therapy on wall-motion score index in patients with ST elevation myocardial infarction-the randomized SOCCER trial. *Echocardiography*. 2017;34(8):1130-1137. doi:10.1111/echo.13599. PMID: 28664557.
21. Khoshnood A, Carlsson M, Akbarzadeh M, et al. Effect of oxygen therapy on myocardial salvage in ST elevation myocardial infarction: the randomized SOCCER trial. *Eur J Emerg Med*. 2018;25(2):78-84. doi:10.1097/MEJ.0000000000000431
22. Sparv D, Hofmann R, Gunnarsson A, et al; DETO2X-SWEDEHEART Investigators. The analgesic effect of oxygen in suspected acute myocardial infarction: A substudy of the DETO2X-AMI Trial. *JACC Cardiovasc Interv*. 2018;11(16):1590-1597. doi:10.1016/j.jcin.2018.04.043
23. Cabello JB, Burls A, Emparanza JI, Bayliss S, Quinn T. Oxygen therapy for acute myocardial infarction. *Cochrane Database Syst Rev*. 2010;(6):CD007160. doi:10.1002/14651858.CD007160.pub2. Update in: *Cochrane Database Syst Rev*. 2013;8:CD007160. PMID: 20556775.
24. Burls A, Emparanza JI, Quinn T, Cabello JB. Oxygen use in acute myocardial infarction: an online survey of health professionals' practice and beliefs. *Emerg Med J*. 2010;27(4):283-286. doi:10.1136/emj.2009.077370
25. Khoshnood A, Carlsson M, Akbarzadeh M, et al. Effect of oxygen therapy on myocardial salvage in ST elevation myocardial infarction: the randomized SOCCER trial. *Eur J Emerg Med*. 2018;25(2):78-84. doi:10.1097/MEJ.0000000000000431
26. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. *Circulation*. 2016;134(10):e123-e155. doi:10.1161/CIR.0000000000000404 Erratum: *Circulation*. 2016;134(10):e192-4. PMID: 27026020.
27. Ibanez B, James S, Agewall S, et al.; ESC Scientific Document Group. 2017 European Society of Cardiology (ESC) Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39(2):119-177. doi:10.1093/eurheartj/ehx393
28. Khoshnood A. High time to omit oxygen therapy in ST elevation myocardial infarction. *BMC Emerg Med*. 2018;18(1):35. doi:10.1186/s12873-018-0187-0
29. Long B, April MD. In patients with acute myocardial infarction and no hypoxemia, does oxygen therapy improve outcomes compared with no supplemental oxygen? *Ann Emerg Med*. 2019;73(4):403-405. doi:10.1016/j.annemergmed.2018.04.015
30. Xin Y, Chen X, Hu W. Oxygen therapy in ST-elevation myocardial infarction. *Eur Heart J*. 2019;40(2):213-214. doi:10.1093/eurheartj/ehy792
31. Fisher J, Wijeysundera DN. Routine supplementary oxygen for myocardial infarction: From unsettled to unsettling. *JACC Cardiovasc Interv*. 2020;13(4):514-516. doi:10.1016/j.jcin.2019.11.010
32. Hofmann R, Abebe TB, Herlitz J, et al.; DETO2X-SWEDEHEART Investigators. Avoiding routine oxygen therapy in patients with myocardial infarction saves significant expenditure for the health care System-insights from the randomized DETO2X-AMI Trial. *Front Public* Health. 2022;12;9:711222. doi:10.3389/fpubh.2021.711222