[Pulmonary Vascular Original Research]

CHEST

Oxygen Therapy in Patients With Intermediate-Risk Acute Pulmonary Embolism

A Randomized Trial

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Background

- Acute pulmonary embolism (PE) is common and sometimes fatal.
- Right ventricle (RV) dysfunction (ie, intermediate-risk PE) at the time of diagnosis is an important determinant of the severity of PE.
- Anticoagulation monotherapy is the current standard treatment for such patients.
- However, short-term PE-related complication rates among patients with intermediate-risk PE may reach 10%; therefore, additional therapeutic approaches are needed.
- Oxygen is a potent and selective pulmonary vasodilator.
- In a porcine model of acute PE mimicking intermediate- to high-risk PE, investigators found that increased oxygen supply decreased RV afterload and lowered its mechanical work.

AIM of the study

To evaluate the effect of oxygen therapy among nonhypoxemic patients with intermediate-risk acute symptomatic PE.

Methods (I)

- Prospective multicenter randomized (1:1), open-label, parallel-group trial .
- The trial was conducted from July 2019 through August 2022 in seven academic hospitals across Spain.
- Adult patients were eligible if they had an objective diagnosis of acute symptomatic PE and an RV to left ventricle (LV) diameter ratio of > 1.0 in the apical four-chamber view on transthoracic echocardiography.
- Patients were excluded if they were receiving chronic oxygen therapy, if they had oxygen saturation of < 90% on pulse oximetry at the time of diagnosis, or had hemodynamic instability at the time of hospital admission.
- Patients were randomized to receive anticoagulation plus supplemental oxygen (through a face mask at a concentration of 35%) for the first 48 h or anticoagulation alone.

Methods (II)

- Trained and certified local cardiologists performed transthoracic echocardiography and measured baseline RV to LV ratio at baseline, after 48 h and after 7 days from baseline.
- The primary outcome was an RV to LV diameter ratio of ≤1.0 from the subcostal or apical view measured 48 h after randomization.
- Secondary efficacy outcomes were the numerical change in the ratio of the RV to LV diameter measured 48 h and 7 days after the start of treatment with respect to the baseline ratio measured at randomization.

Results (I)

- 70 patients, 33 (47%) randomly assigned to the oxygen group and 37 (53%) randomly assigned to the ambient air group.
- Overall, the mean ± SD age was 67.3 ± 16.1 years, and 51% of the patients were female.
- The demographic and clinical characteristics of the patients at baseline did not differ significantly between the two trial groups.
- At baseline, the two treatment groups showed similar echocardiographic mean RV end-diastolic diameter and similar RV to LV ratio.
- No significant difference was found in any of the other baseline echocardiographic right heart parameters between the groups.

Results (II)

- At 48 h after randomization, the primary efficacy outcome was not significantly different in the oxygen group compared with the ambient air group (14 of 33 patients [42.4%] vs 8 of 37 patients [21.6%]; difference, 20.8%; 95% CI, –1.0% to 40.5%; P =.08).
- The proportion of patients with an RV to LV ratio of ≤ 1.0 at 7 days was 76% (25 of 33 patients) and 70% (26 of 37 patients), respectively (difference, 5.5%; 95% CI, –17.2% to 26.9%).
- From baseline to 48 h, the between-group reduction in RV to LV ratio was significantly greater in the oxygen group than in the control group (0.28 0.26 vs 0.12 0.24; P = .02).

Results (III)

During follow-up:

- none of the randomized patients had experienced hemodynamic collapse or recurrent VTE.
- only one case of major bleeding (nonfatal GI bleeding) occurred in a patient in the ambient air group.
- one of the 37 patients randomized to ambient air died of cancer.

TABLE 2] Study Outcomes

Outcome	No. (%) of Patients		*P* Value[a,b]
	Intervention Group (n = 33)	Control Group (n = 37)	
Primary outcome			
48-h echocardiographic RV to LV ≤ 1	14 (42)	8 (22)	.08
Other efficacy outcomes			
7-d echocardiographic RV to LV ≤ 1	25 (76)	26 (70)	1.0
Change in RV to LV ratio			
Baseline minus 48 h	0.28 ± 0.26	0.12 ± 0.24	.02
Baseline minus 7 d	0.41 ± 0.32	0.25 ± 0.23	.06
Change in TAPSE			
Baseline minus 48 h	−2.9 ± 4.5	−1.9 ± 4.7	.44
Baseline minus 7 d	−6.0 ± 3.8	−3.6 ± 4.8	.13
Safety outcomes			
Hemodynamic collapse	0	0	NA
All-cause mortality	0	1 (2.7)	1.0
PE-related mortality	0	0	NA
Major bleeding	0	1 (2.7)	1.0
Minor bleeding	1 (3.0)	3 (8.1)	0.62
Nonfatal recurrent VTE	0	0	NA

Conclusions

- The normalization of the RV to LV ratio in the oxygen group, compared with the ambient air group, did not meet the predetermined level of statistical significance.
- However, oxygen was associated with a greater reduction in RV to LV ratio from baseline to 48 h compared with ambient air.
- Oxygen did not increase clinical adverse events compared with ambient air.
- Findings from this pilot trial support the feasibility of conducting a full-scale randomized controlled trial to evaluate the efficacy of oxygen for nonhypoxemic patients with intermediate-risk PE.