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Review Article

Influence of high-flow nasal cannulae on clinical outcomes in elderly patients with acute respiratory failure: a prognostic risk factor analysis

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Abstract: Objective: To explore the clinical effects of high-flow nasal cannulae (HFNC) in elderly patients with acute respiratory failure (ARF) and analyze prognostic factors following oxygen therapy. Methods: We enrolled 200 ARF patients between January 2022 and June 2023, dividing them into an observation group (n=125) treated with HFNC, and a control group (n=75) receiving conventional oxygen therapy. We compared vital signs before and after treatment and categorized patients into good and poor prognosis groups to analyze demographic data and prognostic factors. Results: Post-treatment, both groups showed improved vital signs, with the observation group experiencing significantly greater improvements ($P<0.05$). However, the observation group had a higher incidence of complications compared to controls ($P=0.001$). Patients with a history of endotracheal intubation or high APACHE II scores were more prevalent in the poor prognosis group (both $P<0.05$). Logistic regression identified the APACHE II score as a risk factor for poor prognosis, while HFNC emerged as a protective factor. Conclusions: HFNC is a safe and effective therapy that improves vital signs and alleviates hypoxia in elderly ARF patients. The APACHE II score and type of oxygen therapy are significant prognostic factors, with HFNC offering a protective effect.

Keywords: High-flow nasal cannulae, acute respiratory failure, poor prognosis, risk factor

Introduction

Acute respiratory failure (ARF) is a severe, often sudden condition predominantly seen in older adults. It is commonly triggered by complications such as severe pneumonia, acute exacerbations of chronic obstructive pulmonary disease (COPD), bronchiectasis, and infections [1-3]. This critical illness can lead to significant ventilation abnormalities or impairments in gas exchange, presenting symptoms like dyspnea and polypnea that may severely impact patient health [4]. Statistical data indicate that millions of Americans suffer from ARF annually, with associated treatment costs reaching approximately $2.7 billion, thus significantly impacting national medical expenditures [5]. ARF is a frequent cause of hospitalizations and intensive care unit (ICU) admissions, emphasizing the importance of early detection and intervention to improve outcomes and reduce complications [6].

Oxygen therapy remains the cornerstone of ARF treatment. Approximately half of ARF patients require invasive mechanical ventilation, which is associated with complications such as ventilator-associated pneumonia and laryngospasm, thereby extending hospital stays and increasing costs. The remaining patients are treated with nasal oxygen therapies, either conventional oxygen therapy (COT) or high-flow nasal cannulae (HFNC), based on their specific needs. Recent studies indicate that HFNC outperforms COT in managing ARF, providing high-flow oxygen through a respiratory humidifier and nasal catheter, which alleviates symptoms rapidly while ensuring comfort and tolerance [7-11]. Reports suggest that HFNC treatment reduces the likelihood of intubation, increases ventilator-free days, and lowers 90-day mortality com-

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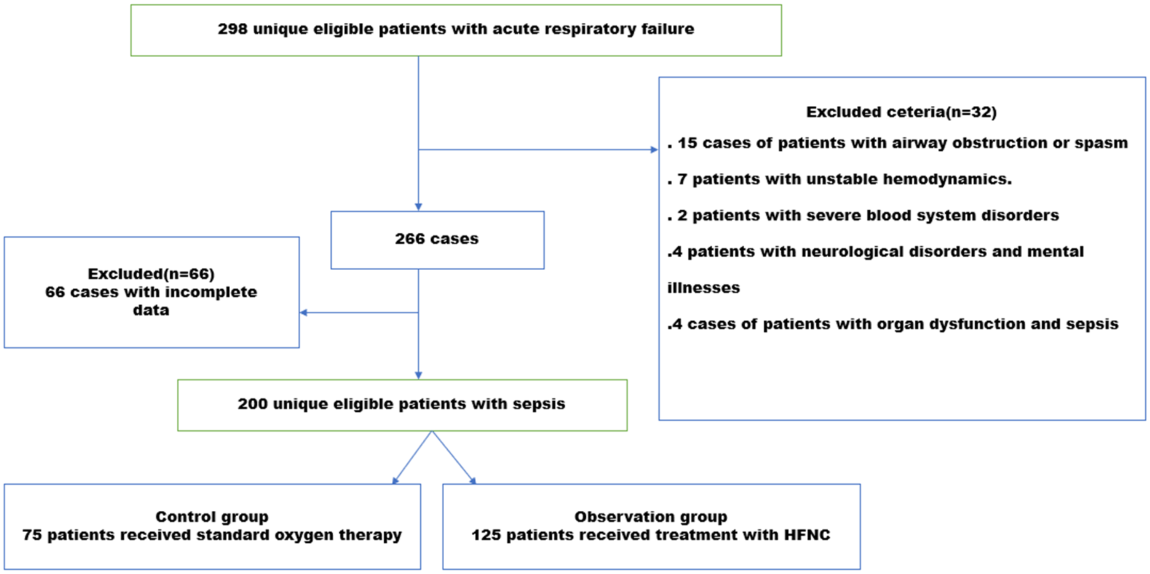

Figure 1. Flow chart of the study.

pared to patients receiving COT or non-invasive ventilation (NIV), highlighting its effectiveness in reducing dependency on mechanical ventilation and improving clinical outcomes [12, 13].

Despite the promising results, existing research predominantly focuses on general populations, with limited studies specifically addressing elderly patients with ARF. This study aims to verify the clinical benefits of HFNC in this age group and contribute new evidence-based insights for optimizing ARF treatment strategies.

Materials and methods

Patient enrollment

A retrospective study was conducted involving 298 ARF patients admitted to Quanzhou First Hospital between January 2022 and June 2023. After screening, 200 patients met the eligibility criteria (**Figure 1**). These were then allocated into two groups: the observation group (n=125) treated with HFNC intervention, and the control group (n=75) receiving COT intervention. The study was approved by the Ethics Committee of Quanzhou First Hospital.

Inclusion criteria

(1) Patients were diagnosed with ARF, characterized by an arterial partial pressure of oxygen (PaO_2) ≤60 mmHg and an oxygenation index ≤300 mmHg. (2) Patients were candidates for oxygen therapy. (3) Patients successfully passed a spontaneous breathing test. (4) Patients had complete medical records, including current and previous data, as well as comprehensive laboratory and imaging results. (5) Patients received oxygen therapy during hospitalization with documented outcomes. (6) Patients were aged 18 years or older.

Exclusion criteria

(1) Presence of conditions like airway obstruction or spasm. (2) Incomplete clinical data. (3) Unstable hemodynamics. (4) Complications with infections or severe hematological disorders. (5) Organ dysfunction, sepsis, or neurological/psychiatric disorders.

Data collection

Treatment protocols for both groups were retrieved from electronic medical records. Upon admission, all patients received routine anti-infective treatments, symptom-targeted management, and supportive care. The prevalent oxygen therapy methods in clinical practice are bubble-type oxygen humidifiers and HFNC. The choice of oxygen therapy was guided by patient preferences, considering the benefits and drawbacks of each method.

Before any endotracheal intubation, each patient received NIV for 5 minutes, with settings including a positive end-expiratory pressure of 5 cmH_2O (1 cmH_2O=0.098 kPa), an inspired oxygen concentration (FiO_2) of 1.0, and a pressure support (PS) of 15 cmH_2O, to maintain arterial oxygen saturation above 90%. Subsequently, the control group received COT with a bubbler humidifier connected to central oxygen supply equipment. The observation group received HFNC, which included adjustments to system temperature (37°C), humidity (100%), oxygen concentration (60%-100%), and flow rate (40-60 L/min), airway pressure (3-4 cmH_2O) to maintain a targeted SpO_2 ≥95% and constant oxygen supply for 24 h, which were performed three times a day, 2 hours each, and adjusted based on patient conditions.

Baseline data such as height, weight, BMI, age, and gender were collected for analysis.

Primary outcome measures

Brain natriuretic peptide (BNP) levels were collected before and three days after treatment using 5 mL of fasting cubital venous blood, analyzed by immunoturbidimetry.

Vital signs including heart rate (HR), mean arterial pressure (MAP), and respiratory rate (RR) were monitored via electrocardiogram upon admission and three days post-treatment.

Blood gasses, such as partial pressure of oxygen in arterial blood (PaO_2), partial pressure of carbon dioxide in arterial blood ($PaCO_2$), as well as their pondus hydrogenii (pH), were assessed using a blood gas biochemical analyzer upon admission and three days later, following strict operational guidelines.

Secondary outcome measures

The incidence of adverse events such as shock, ventricular arrhythmia, severe hypoxemia, and sudden cardiac arrest were observed and recorded post-intervention. Criteria for shock included systolic blood pressure <65 mmHg, or <90 mmHg for ≥30 min, requiring vasoactive drugs after fluid resuscitation. Severe hypoxemia was defined as SpO_2<80% [14].

Statistical analysis

Statistical analysis was conducted using SPSS 22.0. Measurement data were expressed as mean ± standard deviation and analyzed using the t-test for normally distributed data, or the Mann-Whitney U test for non-normally distributed data. Paired sample t-tests were used for within-group comparisons, and independent sample t-tests for between-group comparisons. Count data were analyzed using the χ^2 test and expressed as percentages. Significant variables from univariate analyses were further analyzed using logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs). A *P* value <0.05 was considered statistically significant.

Results

Comparison of baseline data analysis

The baseline data analysis revealed no significant differences between groups in terms of sex, age, disease duration, etiology, history of endotracheal intubation, and APACHE II scores (all P>0.05, **Table 1**).

Comparison of BNP and vital signs

Before the intervention, there were no significant differences in BNP levels, HR, MAP, or RR between the two groups (all P>0.05). Post-intervention, these indices decreased in both groups, with more pronounced reductions observed in the observation group compared to the control group (all P<0.05, **Figure 2**).

Blood gas indexes and pH value analysis

Initial comparisons of PaO_2 and pH levels showed no significant differences between the groups prior to intervention (all P>0.05). Following treatment, there was a significant increase in PaO_2 and reductions in $PaCO_2$ and pH across both groups (all P<0.05). Notably, the observation group exhibited a significantly higher PaO_2 and lower $PaCO_2$ and pH levels in the observation than those in the control group (all P<0.05, **Figure 3**).

Complications analysis

The rate of complications, including shock, ventricular arrhythmia, severe hypoxemia, and sudden cardiac arrest, was assessed for both groups. The incidence rate was 17.60% in the observation and 33.33% in the control (P<0.05, **Table 2**).

Table 1. Comparison of baseline data analysis

Indicators	Observation group (n=125)	Control group (n=75)	χ^2/t	P
Sex			0.023	0.880
Male	78 (62.90)	46 (61.33)		
Female	47 (37.60)	29 (38.67)		
Age (years)	57.70±8.47	57.95±6.23	0.222	0.825
Disease course (h)	20.04±2.99	19.25±2.85	1.841	0.067
Etiology			1.386	0.500
Severe pneumonia	85 (68.00)	56 (74.67)		
Acute exacerbation of COPD	36 (28.80)	16 (21.33)		
Bronchiectasis with infection	4 (3.20)	3 (4.00)		
History of endotracheal intubation			0.594	0.441
Yes	45 (36.00)	23 (30.67)		
No	80 (64.00)	52 (69.33)		
APACHE II score (points)	22.73±3.31	23.13±2.91	0.865	0.388

Note: COPD: chronic obstructive pulmonary disease; APACHE II: Acute Physiology and Chronic Health Evaluation II.

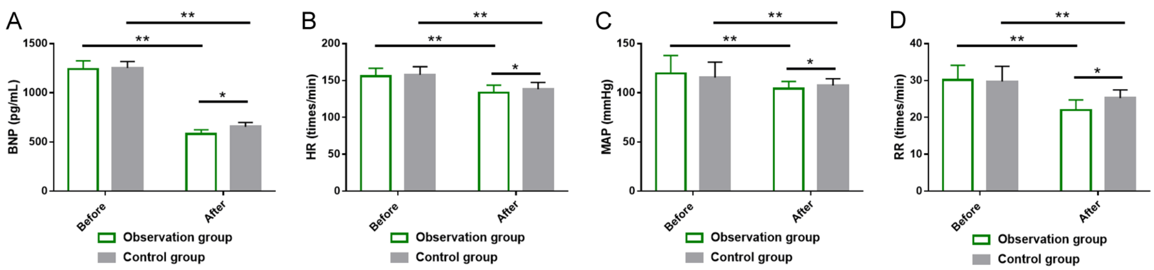

Figure 2. Comparison of BNP, HR, MAP, and RR levels. A: The two groups showed reduced BNP levels after treatment, with a significantly lower BNP level in the observation group than that in the control group. B: The two groups showed reduced HR after treatment, with a significantly lower HR in the observation group than that in the control group. C: The two groups showed reduced MAP after treatment, with a markedly lower MAP level in the observation group than that in the control group. D: Both groups showed markedly reduced RR after treatment, with a significantly lower RR level in the observation group than that in the control group. Note: BNP: Brain natriuretic peptide; HR: heart rate; MAP: mean arterial pressure; RR: respiratory rate. Compared with the observation group, $^*P<0.05$, $^{**}P<0.01$.

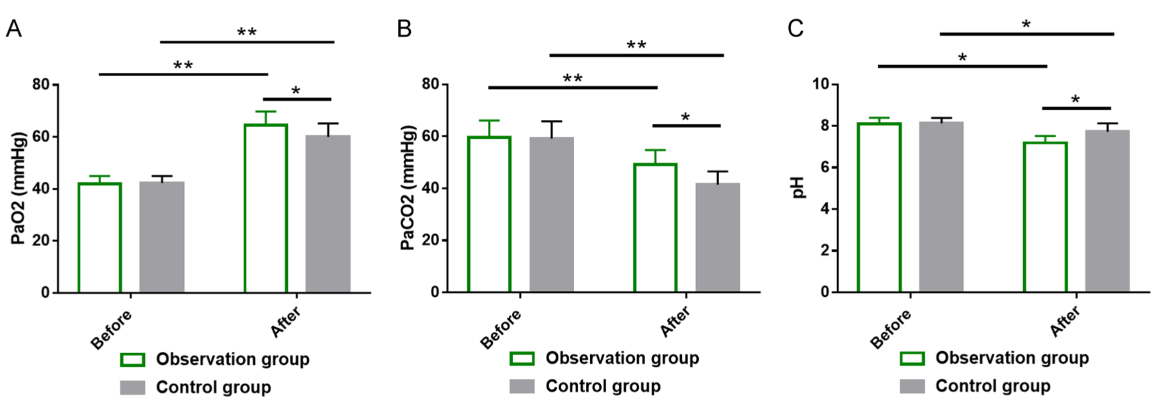

Figure 3. Comparison of blood gas indexes and pH values in the two groups. A: The two groups showed an increase in PaO_2 after treatment, with a markedly higher PaO_2 in the observation group than that in the control group. B: The two groups showed a reduction in $PaCO_2$ after treatment, with a significantly lower $PaCO_2$ in the observation group than that in the control group. C: The two groups showed a decrease in pH after treatment, with a markedly lower pH in the observation group than that in the control group. Note: PaO_2: arterial partial pressure of oxygen; $PaCO_2$: partial pressure of carbon dioxide; pH: pondus hydrogenii. Compared with the observation group, $^*P<0.05$, $^{**}P<0.01$.

Table 2. Comparison of complications

Indicators	Observation group (n=125)	Control group (n=75)	χ^2/t	P
Shock	13 (10.40)	12 (16.00)	1.344	0.246
Ventricular arrhythmia	9 (7.20)	8 (10.67)	0.724	0.395
Severe hypoxemia	0 (0.00)	3 (4.00)		1.000
Sudden cardiac arrest	0 (0.00)	2 (2.67)		1.000
Total	22 (17.60)	25 (33.33)	6.454	0.011

Univariate analysis of poor prognosis in elderly ARF patients receiving oxygen therapy

In this study, elderly ARF patients who developed complications post-oxygen therapy (either HFNC or COT) were classified as the poor prognosis group (n=35), while those without complications were deemed the good prognosis group (n=165). Univariate analysis revealed that gender, age, disease course, and etiology did not significantly influence prognosis (P>0.05). However, a history of endotracheal intubation and high APACHE II scores were significantly associated with poor prognosis in patients undergoing COT (P<0.05, **Table 3**).

Logistic multivariate regression analysis of poor prognosis in elderly ARF patients following HFNC

Variables showing statistical significance in the univariate analysis were included in a logistic regression analysis. The analysis identified a high APACHE II score (P=0.003, OR=4.512, 95% CI: 1.657-12.283) as a risk factor for poor prognosis following HFNC treatment, while HFNC was a protective factor for elderly ARF patients (P=0.001, OR=0.325, 95% CI: 0.112-0.553) (**Tables 4** and **5**).

Discussion

High-flow nasal oxygen technology, a recent innovation in respiratory support, has gained considerable attention for its ability to deliver heated and humidified oxygen at high flow rates via a specialized nasal cannula system. This technology not only improves oxygenation and alleviates breathlessness but also enhances respiratory comfort. HFNC is increasingly utilized as a non-invasive respiratory support in emergency departments for ARF patients, serving as an alternative to COT and NIV. A notable advantage of HFNC is its high tolerability and minimal interference with patients' daily activities, such as eating and communicating, due to its delivery of heated and humidified oxygen through nasal inhalation, optimizing the patient experience [15-17].

This study evaluated the clinical benefits of HFNC in elderly patients with ARF observation control, revealing significant reductions in serum BNP levels post-treatment in both the groups, with more pronounced decreases observed in the observation group. This suggests that HFNC may effectively lower serum BNP levels in this patient population. BNP is a crucial diagnostic biomarker in emergency settings, valuable for assessing the severity and prognosis of ARF and aiding in the diagnosis of shock or heart failure in ICU patients [18, 19]. Notably, decreases in BNP levels have been associated with all-cause mortality in patients with acute heart failure [20]. The beneficial effects of HFNC may be partly derived from its capacity to reduce serum BNP levels, potentially slowing ARF progression.

Furthermore, vital signs such as HR, MAP, and RR significantly improved in both groups after treatment, with more substantial reductions in the observation than in the control group. This indicates that HFNC aids in the recovery of vital signs, likely due to its ability to control oxygen flow and velocity, alongside its continuous positive airway pressure function, which may reduce airway pressure and resistance. Consequently, patients required less ventilator-assisted oxygen due to the high-flow oxygen, enhancing the recovery rate of vital signs. These findings align with previous studies [21, 22].

Additionally, the incidence of hypercapnia was lower in the observation group compared to the control group, further supporting that HFNC improves vital signs in ARF patients, consistent with earlier research [11, 23].

This study found significant improvements in arterial blood gas indices after treatment with HFNC, evidenced by PaO_2 in the observation group, surpassing that in the control group. Conversely, the $PaCO_2$ and pH levels decreased more significantly in the observation, suggesting a superior regulation of acid-base balance

Table 3. Univariate analysis of poor prognosis in elderly ARF patients after oxygen therapies

Indicators	Good prognosis group (n=165)	Poor prognosis group (n=35)	χ^2/t	P
Sex			0.017	0.895
Male	64 (62.14)	14 (63.64)		
Female	39 (37.86)	8 (36.36)		
Age (years)			0.578	0.447
≤58	56 (54.37)	10 (45.45)		
>58 (n=59)	47 (45.63)	12 (54.55)		
Disease course (h)			1.052	0.305
≤20	58 (56.31)	15 (68.18)		
>20 (n=52)	45 (43.69)	7 (31.82)		
Etiology			0.581	0.748
Severe pneumonia (n=85)	69 (66.99)	16 (72.73)		
Acute exacerbation of COPD (n=36)	31 (30.10)	5 (22.73)		
Bronchiectasis with infection (n=4)	3 (2.91)	1 (4.55)		
History of endotracheal intubation			3.986	0.046
Yes (n=45)	33 (32.04)	12 (54.55)		
No	70 (67.96)	10 (45.45)		
APACHE II score (points)			10.643	0.001
≤23	71 (68.93)	7 (31.82)		
>23 (n=47)	32 (31.07)	15 (68.18)		
Treatment protocol			6.984	0.008
COT	55	20		
HFNC	110	15		

Note: ARF: Acute respiratory failure; HFNC: high-flow nasal cannulae; COPD: chronic obstructive pulmonary disease; APACHE II: Acute Physiology and Chronic Health Evaluation II; COT: conventional oxygen therapy.

Table 4. Logistic multivariate regression analysis assignment

Factor	Variables	Assignment
History of endotracheal intubation	X1	Yes =1, no =0
APACHE II score (points)	X2	>23=1, ≤23=0
HFNC	X3	Yes =1, no =0

Note: APACHE II: Acute Physiology and Chronic Health Evaluation II; HFNC: high-flow nasal cannulae.

with HFNC. Elevated PaO_2 indicates improved oxygenation, while unusually high $PaCO_2$ can lead to respiratory acidosis and a high pH (above 7.45) might induce respiratory alkalemia [24-26]. The results indicate that HFNC potentially prevents both respiratory acidosis and alkalosis [27].

Additionally, the most common complications observed were shock and ventricular arrhythmia. Patients in the control group also experienced severe hypoxemia and sudden cardiac arrest more frequently. Notably, the overall complication rate was significantly lower in the observation group, highlighting HFNC's role in control group reducing the risk of adverse outcomes in elderly ARF patients, affirming its safety.

The mechanism underlying the reduction of arrhythmias involves the stabilization of the heart's electrophysiological activity, which is normally governed by specific electrical signals. High-flow oxygen therapy increases the volume and flow rate of inhaled oxygen, enhancing blood oxygen saturation and overall oxygenation, including that of the heart. This improved oxygen delivery stabilizes cardiac electrophysiological activity, thus mitigating arrhythmia risks. Additionally, the adequate supply of oxygen molecules not only improves cardiac oxygenation but also reduces cardiac load and stress, further stabilizing electrophysiological activity. HFNC also diminishes inflammation, contributing to the prevention of arrhythmias [28, 29].

Table 5. Logistic multivariate regression analysis of poor prognosis in elderly ARF patients after oxygen therapies

Factor	B	S.E.	Wald	P	OR	95% CI
History of endotracheal intubation	0.842	0.499	2.849	0.091	2.320	0.873-6.163
APACHE II	1.507	0.511	8.693	0.003	4.512	1.657-12.283
HFNC	1.669	0.662	7.665	0.001	3.325	1.112-0.553

Note: ARF: Acute respiratory failure; HFNC: high-flow nasal cannulae; S.E.: standard error; OR: odd ratio; CI: confidence interval; APACHE II: Acute Physiology and Chronic Health Evaluation II.

The prognostic risk factors for elderly ARF patients were evaluated through univariate and multivariate analyses. First, a significant number of patients with a history of endotracheal intubation exhibited a poor prognosis. Notably, the APACHE II scores were significantly higher in the poor prognosis group than in the good prognosis group. Second, high APACHE II scores and COT were strongly associated with poor outcomes post-treatment. COT, while providing essential oxygen support, is limited in its ability to adjust oxygen flow and concentration. This is particularly problematic for ARF patients requiring high oxygen concentrations, as COT often fails to meet these demands. In contrast, HFNC deliver oxygen at velocities up to 60 L/min, surpassing COT's capabilities. This not only ensures an adequate supply of high-concentration oxygen but also generates a slight positive pressure, reducing airway resistance and enhancing gas exchange efficiency. Additionally, HFNC improves the respiratory tract's temperature and humidity-factors crucial for maintaining mucosal function but often overlooked with COT, leading to dryness and discomfort, and potentially causing mucosal damage. HFNC uses a specialized humidifier to provide body-temperature, fully humidified oxygen, enhancing comfort and reducing complication risks. A high APACHE II score suggests poor overall oxygenation, where non-invasive oxygen therapy fails to achieve desired effects. This is corroborated by previous studies [30, 31]. Furthermore, respiratory rate two hours post-treatment, and FiO_2 and ROX indices eight hours post-treatment, have been identified as useful prognostic indicators after HFNC treatment [29].

The study faces limitations due to the small sample size, affecting the logistic regression model's stability. Future research should include a larger cohort to strengthen these findings. Additionally, the short follow-up period and the self-selection bias in oxygen therapy choice during hospitalization were identified as limitations; longer follow-up and more rigorous research methodologies are recommended to address these issues.

In summary, HFNC intervention effectively reduces serum BNP levels, stabilizes vital signs, maintains arterial blood gas and pH balance, and decreases postoperative complication rates in elderly ARF patients. High APACHE II scores, however, indicate a poor prognosis with HFNC treatment, suggesting that patients with severe conditions may not be suitable candidates for this therapy.

Disclosure of conflict of interest

None.

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