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ORIGINAL RESEARCH **INTENSIVE CARE**

Role of integrated pulmonary index in respiratory monitoring of spontaneously breathing COVID-19 patients with moderate to severe respiratory symptoms

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ABSTRACT

Background & objective: Most of the COVID-19 patients suffered from moderate to severe respiratory symptoms. Many of them needed oxygen supplementation or even mechanical ventilation. There is little data available about the use of either end-tidal CO_2 ($EtCO_2$) or integrated pulmonary index (IPI) in these patients. The aim of this study to investigate the difference in IPI values for subjects requiring mechanical ventilation compared to those managed without ventilation and the correlation between EtCO2 and SpO2.

Methods: This prospective observational study involved adult COVID-19 patients admitted to the ICU withmoderate to severe respiratory symptoms. All patients were connected to a portable respiratory monitor with the IPI algorithm (Medtronic Capnostream 35) and treated according to a standardized protocol. Oxygen flow was adjusted to maintain oxygen saturation (92–96%). If therespiratory rate did not fall below 30 breaths per minute and/or the SpO_2 did not reach the target,non-invasive ventilation (NIV) was initiated. Patients with NIV failure was eligible for invasivemechanical ventilation.

Results: SpO_2 was significantly lower, while RR was significantly higher in intubated group compared to non-intubated group ($P < 0.001$ and 0.018, respectively). However, IPI, $EtCO_2$, and HR did not differ among both groups. There was a significant positive correlation between $EtCO_2$ and SpO_2 at baseline before oxygen therapy ($r = 0.419$; $P = 0.007$). There was a significant negative correlation between CT score and SpO_2 ($r = -0.408$; $P = 0.01$); however, there was no correlation between CT score and both IPI and end tidal CO_2 at baseline ($r = 0.017$; $P = 0.9$).

Conclusion: The integrated pulmonary index cannot be used as a single parameter for assessing respiratory severity in COVID-19 patients.

Abbreviations: $EtCO_2$ - end-tidal CO_2; IPI - integrated pulmonary index; NIV - non-invasive ventilation;

Keywords: Integrated Pulmonary Index, COVID-19, $EtCO_2$, CT severity score.

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1. INTRODUCTION

The most common complication of advanced COVID-19 is acute hypoxemic respiratory insufficiency or failure requiring oxygen and ventilation therapies.[1] The hypoxemic respiratory failure is the marked discrepancy between relatively well-preserved lung compliance and a severely compromised pulmonary gas exchange, leading to grave hypoxemia yet without proportional signs of respiratory distress.[2, 3] The compensatory ventilatory response to hypoxemia, increased minute ventilation, which may lead to extreme hypocapnia and respiratory alkalosis. The physiological hallmarks of respiratory alkalosis are shift of the oxyhemoglobin dissociation curve to the left, thereby increasing hemoglobin's oxygen affinity, evident from a decrease in the P50 value and an increase in arterial oxygen saturation (SaO_2).[4, 5]

The current guideline recommends starting with conventional oxygen therapy to maintain oxygen saturation (SpO_2) at 92% to 96%.[6] However, without knowledge of the accompanying $PaCO_2$ value, it is impossible to infer from SpO2, the degree of hypoxemia and consequently the severity of the respiratory failure.[7]

The FDA-cleared integrated pulmonary index (IPI) algorithm utilizes the real-time measurement and interactions of four parameters ($EtCO_2$, breathing frequency, heart rate, and SpO_2) to provide a rapid assessment of a patient's respiratory status.[8, 9] The algorithm is designed to calculate IPI from various combinations of these measured parameters using a fuzzy logic model that mimics human thinking and associated clinical decision-making based on a group of clinicalexperts.[10, 11] IPI is displayed as a single indexed value from 1 to 10. In a clinical validation study by Ronen et al.,[9] an IPI < 4 was thought to require immediate clinical intervention due to deterioration in the patient's respiratory status..

We investigated the difference in IPI values for COVID-19 patients with moderate to severe respiratory symptoms requiring mechanical ventilation compared to non-ventilated ones as well as the correlation between $EtCO_2$ and SpO_2.

2. METHODOLOGY

This prospective observational study was carried out on 50 patients, aged more than 18 y, from both sexes, with clinical criteria of severe respiratory symptoms defined as fever or suspected respiratory infection plus one of the following: respiratory rate (RR) > 30 breaths/min; severe respiratory distress; or $SpO_2 \leq 93\%$ on room air. The study was done after approval from ethical committee of Faculty of Medicine, Kasr Al-Ainy Teaching Hospital, Cairo, Egypt. Exclusion criteria included patients requiring intubation and mechanical ventilation before ICU admission.

Expired gas sampling lines were attached to the patients upon admission to the ICU. The initial $EtCO_2$, RR, SpO_2, pulse rate, and IPI values were recorded. These parameters were measured until patients were transferred out of the ICU by Capnostream™ 35 (Medtronic, USA.) The device measures the $EtCO_2$ and RR by sampling exhaled gas and the SpO_2 and pulse rate by pulse oximetry. Furthermore, the IPI is calculated automatically from four parameters, and all values are displayed on a screen. The calculation methods use a fuzzy logic inference model based on expert clinical opinions. After the provisional IPI is assigned according to the matrix table of RR and $EtCO_2$, the definite IPI is decided, finally adding the evaluation of SpO_2 and PR. This algorithm was verified by comparison to experts' scoring of clinical scenarios.[9]

All patients were treated according to our standardized respiratory protocol. The oxygen flow was adjusted to maintain an oxygen saturation (SpO_2) of 92%–96%. If the RR did not fall below 30 breaths per minute and/or the SpO_2 did not reach the target, non-invasive ventilation (NIV) was initiated. The following features were considered as NIV failure: worsening of dyspnea, worsening or lack of improvement of hypoxemia (defined as $SpO_2 < 90\%$), persistence of RR > 35 breaths/min, appearance of respiratory acidosis (defined as pH < 7.3 and arterial carbon dioxide tension > 50 mmHg), circulatory shock (defined as the use of a vasopressor to maintain the mean arterial pressure at > 65 mmHg), or altered sensorium. A patient who developed any feature of NIV failure was qualified to receive invasive mechanical ventilation.

2.1. Chest CT severity score

The lungs were divided into the following five zones according to the anatomical structure of the lung: left upper lobe, left lower lobe, right upper lobe, right middle lobe, and right lower lobe. Each lung lobe was assigned a score that was based on the following criteria: score 0 = 0% involvement; score 1 = < 5% involvement; score 2 = 5% to < 25% involvement; score 3 = 25% to < 50% involvement; score 4 = 50% to < 75% involvement; and score 5 = ≥ 75% involvement. The summation of scores provided a semi-quantitative evaluation of overall lung involvement (the maximum CT score for both lungs was 25. [4] All patients underwent CT imaging at hospital admission, and the images were scored by an experienced radiologist who was blinded to the clinical data.

The primary outcome was the difference in IPI values for subjects requiring oxygen therapy compared to those in need of non-invasive ventilation. While the secondary outcomes were the correlation between $EtCO_2$ and SpO_2 at baseline before oxygen therapy, correlation of IPI score with CT severity score; correlation of $EtCO_2$ with CT severity score; need for mechanical ventilation; and ICU length of stay.

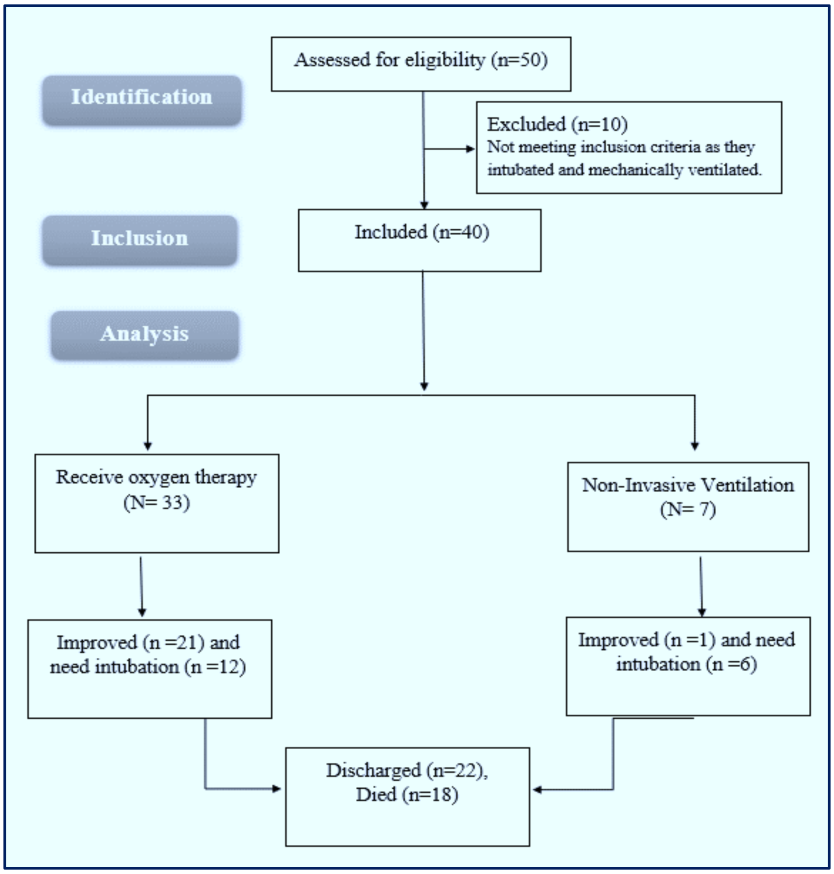

Figure 1: STROBE flow diagram

2.2. Sample size calculation

The sample size calculation was done by G*Power 3.1.9.2 (Universitat Kiel, Germany). According to a previous study,[12] the mean ± SD of IPI (the primary outcome) was 1.47 ± 0.74 in patients with respiratory compromise and 0.93 ± 0.74 in patients without respiratory compromise. The sample size was based on 1.09 effect size, 95% confidence limit, 90% power of the study, and two cases were added to each group to overcome drop out. Therefore, we recruited 40 patients.

2.3. Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Continuous quantitative normally distributed data were expressed as means and standard deviations (SD). Qualitative categorical data were expressed as frequency (%). The correlation was evaluated using the Spearman's correlation coefficient. ROC curve was used to show the diagnostic accuracy.

3. RESULTS

We assessed 50 patients for eligibility; 10 patients were excluded as they needed mechanical ventilation. Forty patients were included in the study. Thirty-three patients received oxygen therapy from the start, while seven patients needed non-invasive ventilation (NIV) (Figure 1).

The patients had a median age of 57 y. Out of 40, 27 (67.5%) patients were males and 13 (32.5%) were females. The mean weight was 100.0 (85.0-107) kg and Charlson Comorbidity Index was 3.0 (1.0 - 4.0) (Table 1).

Table 1: Patients demographic data

Parameter	Value
Age (y)	57.0 (51.0-63.0)
Gender	
• Male	27 (67.5)
• Female	13 (32.5)
Weight (kg)	100.0 (85.0-107)
CCI	3.0 (1.0-4.0)

CCI: Charlson Comorbidity Index; Data presented as median (IQR), or n (%)

There was a significant positive correlation between $EtCO_2$ and SpO_2 ($r = 0.419$; $P < .007$).

Patients who received oxygen therapy had significantly higher SpO_2 and $EtCO_2$ and significantly lower RR and HR compared to patients who received NIV. However, IPI did not differ among both groups (Table 2).

Twenty-one patients who received oxygen therapy and six patients who received an NIV required intubation. In an effort to predict which factor could predict the need for invasive mechanical ventilation, IPI and all its components were compared at baseline on room air. SpO_2 was significantly lower, while RR was significantly higher in intubated groups compared to non-intubated groups ($P < 0.001$ and 0.018), respectively. However, IPI, $EtCO_2$, and HR did not differ among both groups (Table 3).

The cut-off value of the SpO_2 to predict the need for intubation was

Table 2: The Integrated Pulmonary Index (IPI) and its components among study cohort data presented as median

Variable	Non-invasive ventilation (n = 7)	Oxygen therapy (n = 33)	P value
IPI-r	1 (1-1)	3 (1-6)	0.278
SpO_2-r	55 (54-67)	79 (66-83)	0.005*
$EtCO_2$-r	16 (11-17)	19 (15-22)	0.043*
Rr-r	42 (35-55)	33 (29-39)	0.042*
Hr-r	105 (102-114)	86 (77-98)	0.002*

IPI-r: integrated pulmonary index on room air, SpO_2: oxygen saturation, Rr: respiratory rate, Hr: heart rate; P < 0.05 considered as significant

Table 3: The integrated pulmonary index and its components among patients: data presented as median

Variable	Intubated (n = 18)	Non-Intubated (n = 22)	P-value
IPI-r	1 (1-1)	1 (1-1)	0.186
SpO_2-r	66 (55-69)	81 (72-85)	0.000*
$EtCO_2$-r	17 (13-20)	19 (16-25)	0.60
Rr-r	38 (32-55)	32 (27-37)	0.018*
Hr-r	98 (80-103)	86 (79-97)	0.322

IPI: integrated pulmonary index SpO_2: oxygen saturation, $EtCO_2$: end tidal CO_2, Rr: respiratory rate Hr:heart rate; P < 0.05 considered as significant

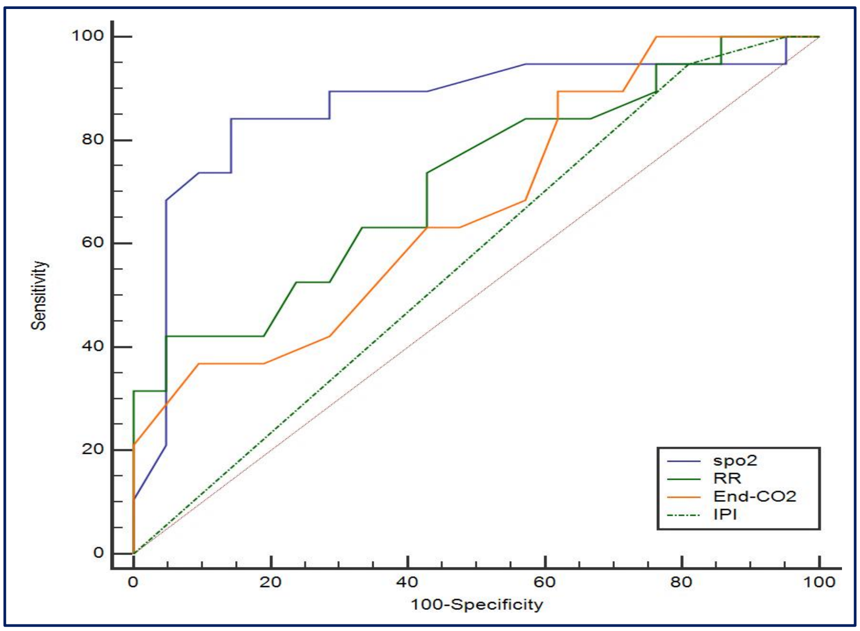

Figure 2: Receiver-operating characteristic curves comparing the abilities of SpO2, RR, EtCO2 and IPI for the need for intubation (SpO_2: peripheral oxygen saturation) RR: respiratory rate, $EtCO_2$: end tidal CO_2; IPI: integrated pulmonary index)

69%, with a sensitivity of 84%, a specificity of 85.7%, and an AUC of 0.8 (95% CI 0.7–0.9, $P < 0.001$). RR showed 0.719 AUC (95% CI: 0.555 to 0.850, $P = 0.018$). $EtCO_2$ showed 0.673 AUC (95% CI: 0.507 to 0.813, $P = 0.06$) (Figure 2).

There was a significant negative correlation between CT score and SpO_2 ($p = 0.01$). However, there was no correlation between CT score and both IPI and $EtCO_2$ at baseline (Table 4). Among the patients who needed mechanical ventilatory support, 18 patients died, which represent 45% of all patients in the study.

Table 4: Correlation between CT score and different parameters

Variable	Correlation coefficient	P value
SpO_2-r	-0.408	0.01*
IPI -r	-0.303	0.07
$EtCO_2$-r	0.017	0.923

SpO_2: oxygen saturation, IPI: integrated pulmonary index, $EtCO_2$: end tidal CO_2 (p value significant < 0.05).

4. DISCUSSION

The IPI was not significantly different between patients requiring oxygen therapy and those requiring non-invasive ventilation (NIV), but all components of IPI were significant. This was due to the fact that the IPI algorithm uses real-time measurements andinteractions of four parameters ($EtCO_2$, RR, HR, and SpO_2) to provide a quick assessment of a patient's respiratory status, and IPI is displayed as a single indexed value ranging from 1 to 10. As the main predictor for IPI was SpO_2, and the median range of SpO_2 in our study was below 85%, the IPI was low (around 1), so the IPI was not significant. according to the calculation methods, which used fuzzy logic inference models.[9]

In our study there was a positive correlation between the end tidal CO2 and SpO_2. $EtCO_2$ levels were lower in patients with the COVID-19 virus who developed tachypnea and hypoxia.[13] This was in line with a study by Hu et al., which examined the relationship between EtCO2 levels and oxygen saturation in COVID-19 patients. [14] They discovered a correlation between the low level of $EtCO_2$ concentration and low oxygen saturation. This is due to breathlessness, poor pulmonary perfusion, and increased alveolar dead space.

In our study, the cut-off value of the SpO_2 to predict the need for intubation was ≤ 69%, with a sensitivity of 84%, specificity of 85.7%, and an AUC of 0.8 (95% CI 0.7–0.9, $P < 0.0001$).

It was in line with Mokhtar et al., who described SpO_2 as a predictor for mechanical ventilation. [15] The cut-off value was ≤ 78%, with a sensitivity of 70% and a specificity of 100%, and the AUC was 0.9 (95% CI 0.8–0.96, $P < 0.0001$). The difference between the cut-off values because in our study we didn't conduct the study on intubated patients, but in Mokhtar et al., they conducted the study between intubated patients and non-invasive ventilation therapy. [15]

In our study, there was no correlation between the IPI and the CT, who described the correlation between the SpO_2 and CT score and revealed that there was a negative correlation between them ($r = -0.6$ and $P < 0.000$), [15] and this is in line with Marco Francone et al., who described the relation between CT score and clinical findings of COVID-19 patients and revealed that CT score is positively correlated with severity of clinical categories and disease phases. [16]

There was no correlation between CT score and $EtCO_2$ in our study. But a study conducted by Hu, D et al.[14], described the correlation between decreased $EtCO_2$ levels and disease severity, and revealed that decreased $EtCO_2$ levels were positively correlated with the severity of the disease. So, we claimed that there was a correlation between CT score and $EtCO_2$ as both values detect the severity of the disease, but this is contrary to our study results

5. LIMITATIONS

The study did not provide power in the investigation between IPI and the mortality rate. The CT score used in our study was based on a scoring system specific to COVID-19 patients and did not use the CT score of ARDS to assess the correlation between the CT score and IPI.

6. CONCLUSION

The integrated pulmonary index cannot be used as a single parameter for assessing the severity of the respiratory status of the COVID-19 patients.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Conflict of interest

The authors declare no conflict of interests, and no external or industry funding was involved.

9. Authors' contribution

SMK: Concept; conduction of the study work
MKA, AMM: Drafting the manuscript; editing.
ASE: Writing study protocol
MAM, SF: Editing of manuscript.
SF: Editing the manuscript.

10. REFERENCES

1. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8:475-81. [PubMed] DOI: 10.1016/S2213-2600(20)30079-5
2. Machluf Y, Rosenfeld S, Ben Shlomo I, Chaiter Y, Dekel Y. The Misattributed and Silent Causes of Poor COVID-19 Outcomes Among Pregnant Women. Front Med (Lausanne). 2021;8:745797. [PubMed] DOI: 10.3389/fmed.2021.745797
3. Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M, et al. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. Intensive Care Med. 2023;49:727-59. [PubMed] DOI: 10.1007/s00134-023-07050-7
4. Vasileiadis I, Alevrakis E, Ampelioti S, Vagionas D, Rovina N, Koutsoukou A. Acid-base disturbances in patients with asthma: A literature review and comments on their pathophysiology. J Clin Med. 2019;8:133-47. [PubMed] DOI: 10.3390/jcm8040563
5. Stewart GM, Cross TJ, Joyner MJ, Chase SC, Curry T, Lehrer-Graiwer J, et al. Impact of Pharmacologically Left Shifting the Oxygen–Hemoglobin Dissociation Curve on Arterial Blood Gases and Pulmonary Gas Exchange During Maximal Exercise in Hypoxia. High Alt Med Biol. 2021;22(3):249-262. [PubMed] DOI: 10.1089/ham.2020.0159
6. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving sepsis campaign: Guidelines on the management of critically ill adults with coronavirus disease 2019 (covid-19). Intensive Care Med. 2020;46:854-87. [PubMed] DOI: 10.1007/s00134-020-06022-5
7. Martínez-Camacho M, Jones-Baro RA, Gómez-González A, Morales-Hernández D, Lugo-García DS, Melo-Villalobos A, et al. Physical and respiratory therapy in the critically ill patient with obesity: a narrative review. Front Med (Lausanne). 2024;11:1321692. [PubMed] DOI: 10.3389/fmed.2024.1321692
8. Siswanto, Gani M, Fauzi AR, Yuliyanti RE, Inggriani MP, Nugroho B, et al. Possible silent hypoxemia in a COVID-19 patient: A case report. Ann Med Surg (Lond). 2020;60:583-6. [PubMed] DOI: 10.1016/j.amsu.2020.11.053
9. Ronen M WR, Overdyk FJ, Ajizian S. Smart respiratory monitoring: clinical development and validation of the IPI™ (Integrated Pulmonary Index) algorithm. J Clin Monit Comput. 2017;31:435-42. [PubMed] DOI: 10.1007/s10877-016-9851-7
10. Improta G, Mazzella V, Vecchione D, Santini S, Triassi M. Fuzzy logic-based clinical decision support system for the evaluation of renal function in post-Transplant Patients. J Eval Clin Pract. 2020;26:1224-34. [PubMed] DOI: 10.1111/jep.13302
11. Adewole KS, Mojeed HA, Ogunmodede JA, Gabralla LA, Faruk N, Abdulkarim A, et al. Expert System and Decision Support System for Electrocardiogram Interpretation and Diagnosis: Review, Challenges and Research Directions. Applied Sci. 2022;12(23).DOI: 10.3390/app122312342
12. Kuroe Y, Mihara Y, Okahara S, Ishii K, Kanazawa T, Morimatsu H. Integrated pulmonary index can predict respiratory compromise in high-risk patients in the post-anesthesia care unit: a prospective, observational study. BMC Anesthesiol. 2021;21:123. [PubMed] DOI: 10.1186/s12871-021-01338-1
13. Ottestad W, Hansen TA, Pradhan G, Stepanek J, Høiseth L, Kåsin JI. Acute hypoxia in a simulated high-altitude airdrop scenario due to oxygen system failure. J Appl Physiol (1985). 2017;123:1443-50. [PubMed] DOI: 10.1152/japplphysiol.00169.2017
14. Hu D, Li J, Gao R, Wang S, Li Q, Chen S, et al. Decreased CO(2) Levels as Indicators of Possible Mechanical Ventilation-Induced Hyperventilation in COVID-19 Patients: A Retrospective Analysis. Front Public Health. 2020;8:596168. [PubMed] DOI: 10.3389/fpubh.2020.596168
15. Mukhtar A, Rady A, Hasanin A, Lotfy A, El Adawy A, Hussein A, et al. Admission SpO(2) and ROX index predict outcome in patients with COVID-19. Am J Emerg Med. 2021;50:106-10. [PubMed] DOI: 10.1016/j.ajem.2021.07.049
16. Francone M, Iafrate F, Masci GM, Coco S, Cilia F, Manganaro L, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. Eur Radiol. 2020;30:6808-17. [PubMed] DOI: 10.1007/s00330-020-07033-y
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