

Limited Clinical Impact of Ultralow-Dose Computed Tomography in Suspected Community-Acquired Pneumonia

Tjitske S. R. van Engelen,^{1,2} Maadrika M. N. P. Kanglie,² Inge A. H. van den Berk,² Josje Altenburg,³ Marcel G. W. Dijkgraaf,⁴ Patrick M. M. Bossuyt,⁴ Jaap Stoker,² and Jan M. Prins¹, on behalf of the OPTIMACT Study Group

¹Department of Internal Medicine, Division of Infectious Diseases, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands, ²Department of Radiology and Nuclear Medicine, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands, ³Department of Pulmonary Medicine, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands, and ⁴Department of Epidemiology and Data Science, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands

Patients clinically suspected of community-acquired pneumonia (CAP) were randomized between ultralow-dose chest computed tomography ([ULDCT] 261 patients) and chest radiograph ([CXR] 231 patients). We did not find evidence that performing ULDCT instead of CXR affects antibiotic treatment policy or patient outcomes. However, in a subgroup of afebrile patients, there were more patients diagnosed with CAP in the ULDCT group (ULDCT, 106 of 608 patients; CXR, 71 of 654 patients; $P = .001$).

Keywords. adult; clinical decision making; emergency service; pneumonia; radiography.

The presence of a parenchymal consolidation on chest x-ray (CXR), combined with systemic signs of infection and symptoms of acute lower respiratory infection, defines a diagnosis of community-acquired pneumonia (CAP) [1]. Performing a CXR is currently the standard diagnostic procedure in patients suspected of CAP. However, chest computed tomography (CT) scan has a higher diagnostic accuracy for CAP compared with CXR [2, 3]. Ultralow-dose chest CT (ULDCT) scans have recently become available, with a radiation dose comparable to

the CXR radiation dose [4, 5]. The ULDCT might therefore replace CXR as the preferred diagnostic procedure in patients clinically suspected of CAP, provided that ULDCT proves to be an accurate diagnostic for CAP, improves antibiotic management, and, most importantly, results in better patient outcomes.

We recently reported on the results of the OPTIMACT study, a large multicenter randomized controlled trial (RCT) designed to evaluate ULDCT versus CXR in patients suspected of non-traumatic pulmonary disease [6, 7]. Short-term functional health was comparable between ULDCT and CXR, as were hospital admissions, length of hospital stay, and mortality rates [7].

However, among the 2418 included patients in this RCT, a higher number of patients was diagnosed with CAP in the ULDCT group, which is in line with previous studies indicating the higher sensitivity of ULDCT [8]. In this study, we investigated whether the higher sensitivity of ULDCT affected clinical management and patient outcomes in the patients clinically (ie, before imaging) suspected of CAP.

METHODS

This is a preplanned subgroup analysis of data prospectively collected in the OPTIMACT trial between January 31, 2017 and May 31, 2018 (The Netherlands Trial Register identifier NTR6163) [6, 7, 9]. Patients in the emergency department (ED) older than 18 years were eligible for inclusion in the OPTIMACT trial if they presented with symptoms of nontraumatic pulmonary disease and required a CXR according to the attending physician. During randomly assigned periods of 1 calendar month, either ULDCT or conventional CXR was used in the 2 participating Dutch hospitals.

Patients were eligible for this preplanned subgroup analysis if there was, before imaging, a clinical suspicion of CAP, defined as at least 1 clinical sign or symptom of an acute lower respiratory tract infection (cough, sputum production, dyspnoea, chest pain, or abnormal breathing sounds at auscultation suggestive of pneumonia), and new onset of systemic infection (fever [$>38^{\circ}\text{C}$] or hypothermia [$<36^{\circ}\text{C}$]). Patients were not eligible in case of a concurrent active infection requiring antibiotic treatment, admission to a hospital in the 2 weeks before ED presentation, or admission to the intensive care unit in the 28 days after ED presentation. Details of the study design and data collection are reported elsewhere [7].

Patient Consent Statement

The Medical Ethics Committee for the Amsterdam University Medical Centers approved the study protocol. The study conforms to ethical standards applied in the Netherlands. Written informed consent was provided by all study participants.

Received 21 December 2022; editorial decision 17 April 2023; accepted 19 April 2023; published online 20 April 2023

Correspondence: Tjitske S. R. van Engelen, MD, Department of Internal Medicine, Division of Infectious Diseases, Amsterdam University Medical Centers, Location AMC, Room G2-105, Meibergdreef 9, 1105 AZ Amsterdam, Netherlands (t.s.vanengelen@amsterdamumc.nl); Jan M. Prins, MD, Department of Internal Medicine, Division of Infectious Diseases, Amsterdam University Medical Centers, Location AMC, Room D3-217, Meibergdreef 9, 1105 AZ Amsterdam, Netherlands (j.m.prins@amsterdamumc.nl).

Open Forum Infectious Diseases®

© The Author(s) 2023. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

<https://doi.org/10.1093/ofid/ofad215>

Table 1. Baseline Characteristics, Diagnosis, and Outcomes

	ULDCT n = 261	CXR n = 231	P Value
General			
Age, year, mean (SD)	57 (19)	58 (18)	
Female sex	126 (48)	104 (45)	
Antibiotic use for RTI or pneumonia before ED presentation	32 (12)	30 (13)	
Comorbidities			
Charlson comorbidity index, ^a median [IQR]	3 [1–5]	3 [1–5]	
Immunocompromised	64 (25)	67 (29)	
Malignancy	45 (17)	51 (22)	
Diabetes	50 (19)	43 (19)	
Pulmonary Diseases			
Chronic obstructive pulmonary disease	36 (14)	36 (16)	
Asthma	33 (13)	21 (9)	
Interstitial lung disease	5 (2)	9 (4)	
Cystic fibrosis	6 (2)	4 (2)	
Cardiac Diseases			
Myocardial infarction	38 (15)	30 (13)	
Chronic cardiac failure	20 (8)	21 (9)	
Neurological diseases	30 (12)	21 (9)	
Kidney disease	23 (9)	23 (10)	
Presenting Symptoms			
Dyspnea	151 (58)	154 (67)	
Cough	191 (73)	174 (75)	
Fever	222 (85)	193 (84)	
Thoracic pain	97 (37)	84 (36)	
Sputum production	99 (38)	96 (42)	
Hemoptysis	13 (5)	13 (6)	
Confusion	8 (3)	11 (5)	
Vital parameters			
Oxygen provided on ED	51 (20)	47 (20)	
Respiratory rate/minute, mean (SD) ^b	21 (6)	20 (6)	
Systolic blood pressure, mmHg, mean (SD)	134 (25)	130 (22)	
Diastolic blood pressure, mmHg, mean (SD)	79 (15)	77 (13)	
Heart rate/minute, mean (SD)	98 (19)	100 (20)	
Temperature, degrees Celsius, mean (SD)	39 (1)	39 (1)	
Severity of Disease			
Pneumonia severity index, median [IQR]	72 [52–98]	77 [53–102]	
Modified early warning score, median [IQR]	3 [2–5]	3 [2–4]	
Definite diagnosis at day 28			
Community-acquired pneumonia	88 (35)	75 (34)	
Bronchitis, bronchiolitis	35 (14)	40 (18)	
Sinusitis and other upper respiratory tract infections	17 (7)	20 (9)	
Pulmonary embolism	1 (0)	5 (2)	
Other pulmonary diseases ^c	67 (26)	66 (29)	
Heart diseases ^d	14 (5)	21 (9)	
Lung cancer or pulmonary metastasis	1 (0)	6 (3)	
Other diagnoses ^e	99 (38)	85 (37)	
Outcomes			
Hospital admission ^f	136 (52)	139 (60)	.09
Length of hospital stay, days, median [IQR] ^g	1.6 [0–5]	1.8 [0–5]	.13
Mortality within 28 days ^f	2 (0.8)	8 (3.5)	.07
Antibiotic treatment in 28 days after ED presentation ^f	165 (63)	155 (67)	.34

Table 1. Continued

	ULDCT n = 261	CXR n = 231	P Value
Total days of antibiotic therapy, median [IQR] ^g	7 [5–9]	7 [5–10]	.68
Functional health ^{b,h,i} , mean (SD)	37 (11)	36 (11)	.30

Abbreviations: CXR, chest radiograph; ED, emergency department; IQR, interquartile range; RTI, respiratory tract infection; SD, standard deviation; ULDCT, ultralow-dose chest computed tomography.

NOTE: Data are n(%) unless otherwise indicated.

^aCharlson comorbidity index, excluding acquired immune deficiency syndrome. Predicts 10-year survival in patients with multiple comorbidities.

^bMore than 5% missing data.

^cAspiration pneumonia, radiation pneumonia, exacerbation asthma, exacerbation chronic obstructive pulmonary disease, exacerbation cystic fibrosis, pleural effusion or empyema, atelectasis, interstitial lung disease.

^dAcute coronary syndrome with or without elevated troponins, stable angina pectoris, cardiac failure, pericarditis, cardiac arrhythmias.

^eAcute chest syndrome in sickle cell disease, thoracic pain of unknown origin, dyspnea of unknown origin, fever of unknown origin, other thoracic pathology, extrathoracic pathology, no pathology, unclear diagnosis.

^f χ^2 test statistic for categorical data.

^gWilcoxon signed-rank sum test for continuous nonparametric data.

^hStudent t test for continuous parametric data.

ⁱBy use of the short form (SF)-12 questionnaire, which measures functional health with the physical component summary scale (PCS) score (scale 0–100, higher score corresponds to better functional health).

We report the proportion of patients who were discharged from the ED with a diagnosis of CAP after initial work up (including imaging) and the proportion of patients who had a definite diagnosis of CAP assigned after 28 days of follow up. We assigned this definite diagnosis based on a review of all clinical, radiological, and microbiological data available after 28 days of follow up [10]. A definite diagnosis of CAP was defined as an acute infection of the respiratory tract (criteria defined above) and a parenchymal lung consolidation on ULDCT or CXR, and it was based on consensus by an adjudication committee using a diagnostic handbook we developed for standardized and reproducible categorization of diagnoses [10].

In an exploratory analysis we used a broader definition of suspected CAP, by also including patients with a temperature between 36°C and 38°C. Outcome measures were number of patients admitted to the hospital, total antibiotic use over 28 days, length of hospital stay, mortality, and functional health at day 28 after ED presentation represented by the short form (SF)-12 questionnaire score.

RESULTS

In the OPTIMACT trial, 2418 patients with nontraumatic pulmonary disease were included. Of those, 492 patients were clinically suspected of having CAP and were included in the current analysis (mean age 58 [standard deviation ± 19] years; 53% male). Two hundred sixty-one patients were allocated to ULDCT and 231 to CXR for radiological examination. Baseline characteristics were comparable between groups (Table 1).

After imaging, 78 of the 261 clinically suspected CAP patients in the ULDCCT group were discharged from the ED with the diagnosis CAP (31%), compared with 75 of 231 (34%) in the CXR group ($P = .6$; χ^2 test). After evaluation of all available data after 28 days of follow up, in the ULDCCT group 88 of the 261 clinically suspected CAP patients were diagnosed with definite CAP (35%), compared with 75 of 231 (34%) in the CXR group ($P = .8$; χ^2 test). Differences between groups in hospital admission, length of hospital stay, mortality, proportion of patients treated with antibiotics, median number of days of antibiotic treatment (days on therapy), and functional health at day 28 were not detected (P values not significant) (Table 1).

In the OPTIMACT trial, we reported a higher number of patients with CAP in the ULDCCT group, both at ED discharge and after 28 days of follow up (definite CAP) [7]. To explain this discrepancy with the current analysis, we hypothesized that the higher diagnostic accuracy of ULDCCT over CXR is mainly relevant in a subset of patients with CAP, such as patients with incipient CAP or an atypical clinical presentation of CAP.

Therefore, in an exploratory analysis, we selected patients with signs or symptoms of an acute lower respiratory tract infection (as defined above) but a temperature between 36°C and 38°C. This resulted in 1262 patients, of which 608 patients were allocated to the ULDCCT group and 654 patients to the CXR group. Of the 1262 patients selected by these exploratory criteria, 106 of 608 patients in the ULDCCT group were discharged from the ED with CAP (18%), compared with 71 of 654 (12%) in the CXR group ($P = .001$; χ^2 test). After evaluation of all available data at day 28, in the ULDCCT group 105 of 608 patients were diagnosed with definite CAP (18%), compared with 70 of 654 (11%) in the CXR group ($P = .001$; χ^2 test).

DISCUSSION

In this study of patients clinically suspected of CAP at ED presentation, we found no benefit in using ULDCCT as a first-line diagnostic procedure compared with using CXR regarding the proportion of patients diagnosed with CAP. Both at discharge from the ED, as well as after reviewing all available clinical data at day 28, the number of patients with a CAP diagnosis was not significantly different between groups. This refuted our hypothesis that the higher diagnostic accuracy of ULDCCT leads to a higher number of patients diagnosed with CAP. In line with this finding, we also did not observe differences in antibiotic consumption or clinical outcome measures, such as hospital admission, length of hospital stay, mortality, and functional health after 28 days.

Claessens et al [3] assessed whether early multidetector chest CT scan affects diagnosis of patients visiting the ED with suspected CAP, and they found it alters antibiotic management. However, Claessens et al [3] used slightly different criteria to

define clinically suspected CAP. Nevertheless, we report on a more heterogenous population, as represented by proportion definite CAP in both cohorts (51% vs 33%).

In a study on pneumonia in elderly patients, the probability of pneumonia was assessed before and after a low-dose CT (LDCT) scan and subsequently compared to the reference diagnosis made by an adjudication committee [11]. The LDCT modified the estimated probability of pneumonia in 45% of patients. Correct reclassification was mainly observed in patients not having pneumonia according to the adjudication committee, suggesting that the potential benefit of the LDCT would mainly lie in reducing overdiagnosis of pneumonia [11].

In the OPTIMACT trial, we reported a higher number of patients with CAP in the ULDCCT group. In an exploratory analysis, we only found a higher number of CAP patients in the ULDCCT group among those with signs and symptoms of an acute respiratory infection but a temperature between 36°C and 38°C. Apparently, the higher proportion of CAP patients in the ULDCCT group versus the CXR group in the OPTIMACT trial was mainly driven by a higher number of CAP patients in the afebrile subset of patients. This can be considered an interesting finding, because this is the group more likely to receive unnecessary antibiotics, and the increased sensitivity of ULDCCT could help rule out disease more effectively.

Based on data from literature and results presented in the present study, one could argue that the value of ULDCCT seems most pronounced among those patients whose clinical presentation is not straightforward, such as patients who are elderly or afebrile. It should be the subject of further studies to identify which groups of patients would benefit most from standard ULDCCT imaging.

Our analysis has limitations. First, even when ULDCCT would not lead to more CAP diagnoses compared with CXR, it could still lead to more accurate CAP diagnoses. Studies in which both CT and CXR were performed in one patient showed that the probability of pneumonia increased in some patients and decreased in others [3, 11]. Second, the coronavirus disease 2019 pandemic may have changed the incidence, presentation, and management of patients suspected of CAP, which is not accounted for in our study. Third, despite the fact that this was a representative cross-section sample of the ED population of 2 large Dutch hospitals, the results of this study cannot be translated directly to specific subgroups, such as the very old.

CONCLUSIONS

In summary, in this randomized trial, we found no indication that performing ULDCCT instead of CXR in febrile or hypothermic patients clinically suspected of CAP at the ED affects antibiotic treatment or patient outcomes. In afebrile patients, however, ULDCCT might have a higher sensitivity to diagnose CAP compared with CXR.

Acknowledgments

We thank the patients and patient representatives who were involved in the OPTIMACT study. We kindly acknowledge all members of the OPTIMACT study group: Jouke Annema, Ludo F. M. Beenen, Dominique Bekebrede-Kaufman, Joost W. van den Berg, Sophie J. Bernelot Moens, Shandra Bipat, Bart G. Boerrigter, Marije M. K. Bomers, Marjolein A. W. van den Boogert, Merel L. J. Bouwman, Paul Bresser, Annemieke K. van den Broek, Brenda Elzer, Jos Donkers, Elvin Eryigit, Betty Frankemölle, Nina-Suzanne Groeneveld, Maarten Groenink, Emo E. van Halsema, Naomi M. Haverkamp Begemann, Suzanne M. R. Höchheimer, David ten Hoff, Frits Holleman, Erwin Hoolwerf, Dorine Hulzebosch, Mitran Keijzers, Saskia Kolkman, Jos A. J. Kooter, Daniel A. Korevaar, Ivo van der Lee, Nick H. J. Lobe, Peter A. Leenhouts, Ramon B. van Loon, Paul Luijendijk, Melanie A. Monraats, Bregje Mol, Jan Luitse, Lilian J. Meijboom, Carmen M. Melaan, Saskia Middeldorp, Alexander Montauban van Swijndregt, Wouter de Monyé, Jacqueline Otker, Anna Pijning, Tom van der Poll, Adrienne van Randen, Tom D. Y. Reijnders, Milan L. Ridderikhof, Johannes A. Romijn, Jorien M. van Rooijen, Maeke J. Scheerder, Antoinet J. N. Schoonderwoerd, Laura J. Schijf, Frank F. Smithuis, Ralf W. Sprengers, Robin Soetekouw, Geert J. Streekstra, Elizabeth M. Taal, Milou M. Tjong Joe Wai, Merve S. Tulek, Glenn de Vries, Daphne D. L. van der Velden, Saskia Veldkamp, Loek Verdegaal, Maaïke J. A. Vogel, Lonneke A. van Vught, Mart Vuurboom, Guus A. Westerhof, Pieta C. Wijsman, Michiel M. Winter, Rosa D. Wouda, and Ibtisam Yahya.

Author contributions. JS, JMP, IAHvdB, MMNPK, PMMB, MGWD, and TSRvE were involved in design, planning and execution, and data interpretation of the main trial. For further details, please see the main paper of the OPTIMACT trial [8]. JMP was the principal investigator of this pre-planned subgroup analysis of the OPTIMACT trial. TSRvE performed the analyses. TSRvE and JMP drafted the manuscript. All authors were involved in data interpretation, critically revised the manuscript, approved the final version of the manuscript, and all agree to be accountable for all aspects of this trial. TSRvE attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. TSRvE had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Disclaimer. The Amsterdam University Medical Centers (UMC) and the Netherlands Organization for Health Research and Development (ZonMW) had no role in the design and conduct of the study, the collection, management, analysis, and interpretation of the data, the preparation, review, or approval of the manuscript, or the decision to submit the manuscript for publication.

Financial support. This work was supported by an innovation grant from the Amsterdam UMC, location Academic Medical Center (AMC),

University of Amsterdam (to MMNPK, IAHvdB, and JS), and a Health Care Efficiency Program grant from the Netherlands Organization for Health Research and Development ([ZonMW] 843001806; to MMNPK, IAHvdB, and JS).

Potential conflicts of interest. TSRvE reports personal fees (a PhD Scholarship grant) from Amsterdam UMC. MMNPK, IAHvdB, and JS received an innovation grant from the Amsterdam UMC, location AMC, University of Amsterdam, and a grant from the Health Care Efficiency Program of the Netherlands Organization for Health Research and Development (ZonMW). Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Prina E, Ranzani OT, Torres A. Community-acquired pneumonia. *Lancet* **2015**; 386:1097–108.
2. Self WH, Courtney DM, McNaughton CD, Wunderink RG, Kline JA. High discordance of chest x-ray and computed tomography for detection of pulmonary opacities in ED patients: implications for diagnosing pneumonia. *Am J Emerg Med* **2013**; 31:401–5.
3. Claessens YE, Debray MP, Tubach F, et al. Early chest computed tomography scan to assist diagnosis and guide treatment decision for suspected community-acquired pneumonia. *Am J Respir Crit Care Med* **2015**; 192:974–82.
4. Ludes C, Schaal M, Labani A, Jeung M-Y, Roy C, Ohana M. Ultra-low dose chest CT: the end of chest radiograph? *Presse Med* **2016**; 45:291–301.
5. Kim Y, Kim YK, Lee BE, et al. Ultra-low-dose CT of the thorax using iterative reconstruction: evaluation of image quality and radiation dose reduction. *Am J Roentgenol* **2015**; 204:1197–202.
6. van den Berk IAH, Kanglie MMNP, van Engelen TSR, et al. OPTimal IMAGING strategy in patients suspected of non-traumatic pulmonary disease at the emergency department: chest X-ray or ultra-low-dose CT (OPTIMACT)—a randomised controlled trial chest X-ray or ultra-low-dose CT at the ED: design and rationale. *Diagnostic Progn Res* **2018**; 2:20.
7. van den Berk IAH, Kanglie MMNP, van Engelen TSR, et al. Ultra-low-dose CT versus chest X-ray for patients suspected of pulmonary disease at the emergency department: a multicentre randomised clinical trial. *Thorax* **2022**; 78:515–22.
8. Kroft LJM, van der Velden L, Girón IH, Roelofs JJH, de Roos A, Geleijns J. Added value of ultra-low-dose computed tomography, dose equivalent to chest X-ray radiography, for diagnosing chest pathology. *J Thorac Imaging* **2019**; 34:179–86.
9. Kanglie MMNP, Bipat S, van den Berk IAH, et al. OPTimal IMAGING strategy in patients suspected of non-traumatic pulmonary disease at the emergency department: chest X-ray or ultra-low-dose chest CT (OPTIMACT) trial—statistical analysis plan. *Trials* **2020**; 21:407.
10. van Engelen TSR, Kanglie MMNP, van den Berk IAH, et al. Classifying the diagnosis of study participants in clinical trials: a structured and efficient approach. *Eur Radiol Exp* **2020**; 4:44.
11. Prendki V, Scheffler M, Huttner B, et al. Low-dose computed tomography for the diagnosis of pneumonia in elderly patients: a prospective, interventional cohort study. *Eur Respir J* **2018**; 51:1702375.