

ORIGINAL ARTICLE

Low-Dose Abdominal CT for Evaluating Suspected Appendicitis

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ABSTRACT

BACKGROUND

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N Engl J Med 2012;366:1596-605.
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Computed tomography (CT) has become the predominant test for diagnosing acute appendicitis in adults. In children and young adults, exposure to CT radiation is of particular concern. We evaluated the rate of negative (unnecessary) appendectomy after low-dose versus standard-dose abdominal CT in young adults with suspected appendicitis.

METHODS

In this single-institution, single-blind, noninferiority trial, we randomly assigned 891 patients with suspected appendicitis to either low-dose CT (444 patients) or standard-dose CT (447 patients). The median radiation dose in terms of dose-length product was 116 mGy-cm in the low-dose group and 521 mGy-cm in the standard-dose group. The primary end point was the percentage of negative appendectomies among all nonincidental appendectomies, with a noninferiority margin of 5.5 percentage points. Secondary end points included the appendiceal perforation rate and the proportion of patients with suspected appendicitis who required additional imaging.

RESULTS

The negative appendectomy rate was 3.5% (6 of 172 patients) in the low-dose CT group and 3.2% (6 of 186 patients) in the standard-dose CT group (difference, 0.3 percentage points; 95% confidence interval, -3.8 to 4.6). The two groups did not differ significantly in terms of the appendiceal perforation rate (26.5% with low-dose CT and 23.3% with standard-dose CT, $P=0.46$) or the proportion of patients who needed additional imaging tests (3.2% and 1.6%, respectively; $P=0.09$).

CONCLUSIONS

Low-dose CT was noninferior to standard-dose CT with respect to negative appendectomy rates in young adults with suspected appendicitis. (Funded by GE Healthcare Medical Diagnostics and others; ClinicalTrials.gov number, NCT00913380.)

OWING TO THE MANY ADVANTAGES THAT computed tomography (CT) has over other diagnostic tests, including ultrasonography,¹⁻³ CT has assumed a paramount position in the evaluation of adults with suspected appendicitis. Despite historical debate,⁴ the increased use of CT has been consistently found to coincide with a reduction in the rate of negative (unnecessary) appendectomies without an increase in the rate of appendiceal perforations — two important reciprocal measures of quality of care that represent, respectively, a false positive diagnosis and a delayed diagnosis.⁵⁻¹⁰ The routine use of CT in patients suspected of having appendicitis has also been reported to be cost-effective, since it prevents delayed or inaccurate diagnoses.¹¹

Many patients in whom appendicitis is suspected are children or young adults,¹² and radiation exposure from CT is of particular concern in this population. Although the issue is debatable, concern that even a single typical abdominal CT examination may confer a small but real risk of carcinogenesis is increasing.^{13,14} No formal guideline has been suggested regarding the optimal radiation dose, but several exploratory studies have shown that reducing the radiation dose by 50 to 80% does not significantly hinder the diagnosis of appendicitis.¹⁵⁻¹⁷ Low-dose CT techniques have not gained wide acceptance because of concern that the increased image noise will degrade image quality. In response to the more frequent use of CT and the increased awareness of its associated carcinogenic risk, the need for a randomized, controlled trial to establish the role of low-dose CT in diagnosing appendicitis has recently been suggested.^{16,18} In the trial reported here, the negative appendectomy rate after low-dose abdominal CT was compared with that after standard-dose abdominal CT among young adults with suspected appendicitis.

METHODS

STUDY DESIGN AND OVERSIGHT

The study was a noninferiority, single-institution, randomized trial. The institutional review board approved the study protocol, available with the full text of this article at NEJM.org. All diagnostic and treatment procedures, except for the CT radiation dose, adhered to the standards of practice followed at the study center, an urban tertiary care hospital in Korea. All the authors designed

the study, gathered and analyzed the data, and vouch for the accuracy and completeness of the data and the fidelity of the study to the protocol. The corresponding author wrote the first draft of the manuscript, and all the authors participated in subsequent revisions and made the decision to submit the manuscript for publication. GE Healthcare Medical Diagnostics, Korea, had no role in the study other than providing grant support.

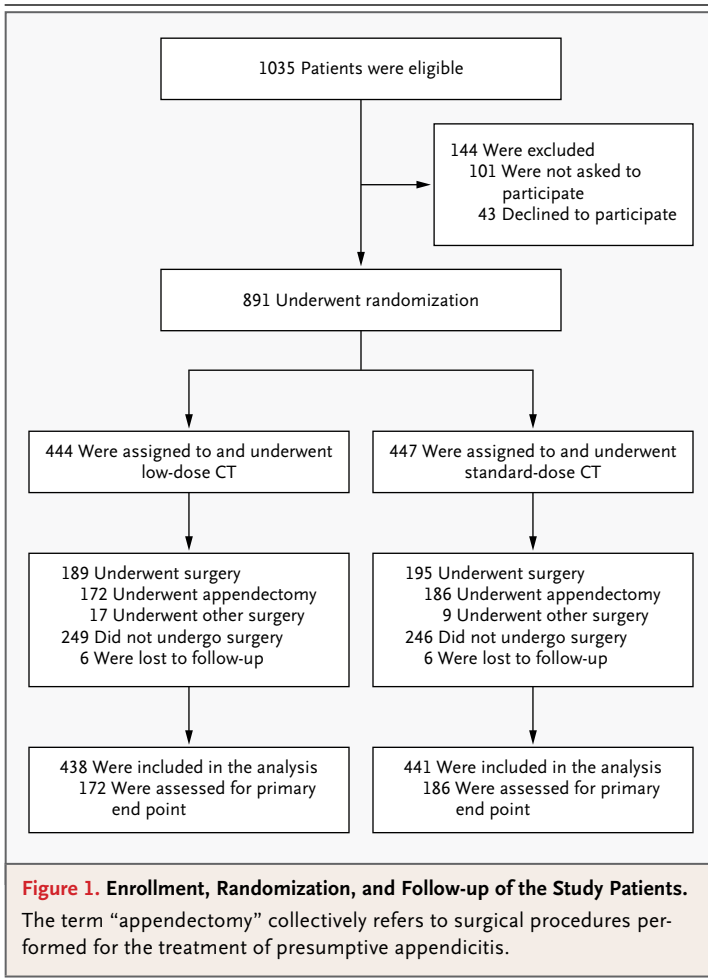
INCLUSION CRITERIA AND RANDOMIZATION

Patients 15 to 44 years of age who were undergoing CT examination for suspected appendicitis were eligible to participate (Fig. 1). (For more details, see the Supplementary Appendix, available at NEJM.org.) Instead of using specific eligibility criteria, we relied on assessments carried out by the emergency department physicians on service that led to the clinical suspicion of appendicitis and the referral of patients for CT examination. This approach was intended to reflect the practice pattern at the investigating center and presumably at many other institutions. Other eligibility criteria included no prior cross-sectional imaging test to evaluate presenting symptoms or signs, no history of appendectomy, and no contraindications to CT performed with the use of intravenous contrast material. In general, ultrasonography instead of CT was recommended for slender patients (those with a body-mass index [the weight in kilograms divided by the square of the height in meters] of less than 18.5), although this characteristic did not constitute an absolute criterion for exclusion.

Patients who gave written informed consent were randomly assigned to undergo either low-dose or standard-dose CT of the abdomen in a 1:1 ratio. Although the care providers were aware of group assignments owing to obvious differences in the texture of the CT images, neither the patients nor the outcome assessors were aware of these assignments.

CT PROTOCOL

Intravenous contrast-enhanced images were obtained with the use of CT scanners with 16, 64, or 256 detector rows. The reference tube current-time product was empirically set, aiming at effective radiation doses of 2 mSv in the low-dose group and 8 mSv in the standard-dose group.¹⁹ (The standard radiation dose was within the range of the often-cited reference values of 7 to 10 mSv.²⁰⁻²²) The actual radiation dose, which was automatically ad-



justed according to the patient’s body size,²³ was recorded in terms of the dose–length product (an indicator of the integrated radiation dose of an entire CT scan). Other scan results were the same for the two groups. In addition to the routine reviews of CT images that were 5 mm thick, images with a thickness of 2 mm were reviewed as needed with the use of the multiplanar sliding-slab averaging technique (as described in the Supplementary Appendix). Technical details are provided in the study protocol.

REPORTS OF CT RESULTS

During the daytime, CT reports were initially prepared by one of three expert radiologists who had participated in the previous research on low-dose CT of the abdomen.^{16,17,24} For CT examinations performed after hours, preliminary reports were provided by on-call radiologists who had various levels of expertise regarding abdominal scans,

including attending radiologists, fellows, and residents, and most of these assessors had limited experience in interpreting the low-dose CT images. The preliminary reports were supplemented by additional reports from the expert radiologists; however, these addenda were not included in the outcome analyses, since we could not objectively determine how they might affect clinical decisions. All interpreting radiologists were allowed to access clinical and laboratory findings and to consult with the referring physician. CT reports conformed to a predefined structured format, indicating the likelihood of appendicitis on a five-point Likert scale and the presence or absence of appendiceal perforation (see the Supplementary Appendix).

ADDITIONAL ABDOMINAL IMAGING TESTS

If the diagnosis of appendicitis remained indeterminate after the initial CT examination and clinical observation, additional abdominal ultrasonography^{25,26} or standard-dose CT could be performed at the discretion of the physician or surgeon on service. An additional imaging test was defined as one performed within 7 days after the initial CT examination to either diagnose or rule out appendicitis.

FINAL DIAGNOSIS

In patients undergoing abdominal surgery, a final diagnosis was made on the basis of surgical and pathological findings. Pathological examinations were performed by pathologists who were not aware of group assignments. In patients not undergoing surgery, independent assessors who were unaware of the group assignments determined the final diagnosis on the basis of medical records and telephone interviews 3 months after the patient’s initial presentation. Details of the reference standard are provided in the Supplementary Appendix.

END POINTS

The primary end point was the rate of negative appendectomy (i.e., the percentage of all nonincidental appendectomies in which the appendix was not inflamed). The secondary end points for clinical outcomes included the rate of appendiceal perforation (i.e., the percentage of all cases of confirmed appendicitis in which the appendix was perforated), the proportion of patients who required additional imaging tests, the interval be-

tween acquisition of the CT images and nonincidental appendectomy or hospital discharge without surgery, and the length of the hospital stay associated with the appendectomy.

Secondary end points with regard to the CT reports were the diagnostic performance for appendicitis in terms of the area under the receiver-operating-characteristic curve (AUC), sensitivity and specificity (with a grade of 3 or higher on the five-point Likert scale considered to be positive for the diagnosis of appendicitis²⁷), and diagnostic confidence (i.e., likelihood of appendicitis), as well as the sensitivity and specificity of CT for the diagnosis of appendiceal perforation. (Definitions of these end points can be found in the Supplementary Appendix.)

STATISTICAL ANALYSIS

The noninferiority margin for the difference in negative appendectomy rates between the two study groups was set as 5.5 percentage points on the basis of an assumption of a 2.5% negative appendectomy rate with standard-dose CT and a judgment that a negative appendectomy rate of 8% is clinically acceptable with low-dose CT. To obtain 90% statistical power with a two-sided alpha value of 0.05, the trial was continued until the number of nonincidental appendectomies per group exceeded 170. Patients not undergoing appendectomy during the study period were also included in the study. (Further details of the sample-size calculation are available in the Supplementary Appendix.)

Patients undergoing randomization were included in the analysis in the groups to which they were originally assigned. A two-sided 95% confidence interval for the difference in negative appendectomy rates was calculated to test for noninferiority. Fisher's exact tests, Mann-Whitney U tests, and receiver-operating-characteristic analysis were used for the secondary end points. A two-sided P value of less than 0.05 was considered to indicate statistical significance.

RESULTS

PATIENTS

From September 2009 through January 2011, a total of 1035 patients were identified as eligible for the study by 7 attending physicians and 43 physicians in training in the emergency department; 891 patients (including 886 Koreans) who

gave informed consent were randomly assigned to either low-dose CT (444 patients) or standard-dose CT (447 patients) (Fig. 1). Six patients in each group were lost to follow-up after discharge without appendectomy. The remaining 438 patients in the low-dose CT group and 441 in the standard-dose CT group were included in the outcome analyses. The baseline characteristics of the two groups are shown in Table 1.

CT EXAMINATION

The median dose-length product was 116 mGy-cm (interquartile range, 94 to 124) and 521 mGy-cm (interquartile range, 448 to 564) for each group (see the Supplementary Appendix). Three expert radiologists prepared reports for 217 of the 444 patients in the low-dose CT group and for 225 of the 447 patients in the standard-dose CT group; reports for the remaining CT examinations were made by 14 other attending radiologists and 36 trainees.

ADDITIONAL IMAGING TESTS

The proportion of patients who required additional imaging tests was 3.2% (14 of 438) in the low-dose CT group and 1.6% (7 of 441) in the standard-dose CT group (P=0.09) (Table 2, and the Supplementary Appendix).

APPENDECTOMY OR DISCHARGE WITHOUT SURGERY

Nonincidental appendectomy was performed in 172 patients in the low-dose CT group and 186 in the standard-dose CT group and involved 13 attending surgeons, whereas 249 patients in the low-dose CT group and 246 in the standard-dose CT group were discharged without surgery. Table 2 shows the interval between CT-image acquisition and appendectomy or hospital discharge without surgery, as well as the length of the hospital stay associated with nonincidental appendectomy. (Details about the surgical procedures and the time to patient disposition are provided in the Supplementary Appendix.)

FINAL DIAGNOSIS

Pathological examinations were performed by seven pathologists. Appendicitis was confirmed in 166 of 438 patients in the low-dose CT group (37.9%) and 180 of 441 in the standard-dose CT group (40.8%). The remaining patients were considered not to have appendicitis on the basis of negative findings in appendectomy specimens (in 18 cases),

the gross appearance of the appendix during surgery without appendectomy (in 20 cases), or medical records and telephone interview (in 495 cases). In 72 patients in the low-dose CT group and 86 in the standard-dose CT group, a diagnosis other than nonspecific abdominal pain or nonspecific gastroenterocolitis was established (see the Supplementary Appendix).

NEGATIVE APPENDECTOMY RATE AND APPENDICEAL PERFORATION RATE

The negative appendectomy rate was 3.5% (6 of 172 patients) in the low-dose CT group, as com-

pared with 3.2% (6 of 186 patients) in the standard-dose CT group, for an absolute difference of 0.3 percentage points (95% confidence interval [CI], -3.8 to 4.6) and a relative risk of 1.08 (95% CI, 0.37 to 3.13) (Table 2). Since the upper boundary of the two-sided 95% confidence interval lay below the predefined noninferiority margin, the noninferiority of low-dose CT to standard-dose CT was established. The distribution of negative appendectomies according to baseline characteristics of the patients, type of CT scanner, radiologist's expertise, and use of a laparoscopic or an open approach is shown in Table 3. (Details concerning

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Low-Dose CT Group (N=444)	Standard-Dose CT Group (N=447)
Age — yr		
Median	29	30
Interquartile range	22–36	22–37
Sex — no. (%)		
Female	276 (62.2)	263 (58.8)
Male	168 (37.8)	184 (41.2)
Body-mass index — no. (%)†		
<18.5 (underweight)	62 (14.0)	60 (13.4)
18.5–24.9 (normal)	312 (70.3)	301 (67.3)
25.0–29.9 (overweight)	67 (15.1)	76 (17.0)
30.0–34.9 (class I obesity)	3 (0.7)	9 (2.0)
35.0–39.9 (class II obesity)	0	1 (0.2)
≥40.0 (class III obesity)	0	0
Chief symptom — no. (%)		
Abdominal pain	421 (94.8)	430 (96.2)
Other	23 (5.2)	17 (3.8)
Duration of symptoms — no. (%)		
≤12 hr	157 (35.4)	151 (33.8)
13–24 hr	167 (37.6)	158 (35.3)
2–3 days	84 (18.9)	101 (22.6)
≥4 days	36 (8.1)	37 (8.3)
Location of pain — no. (%)		
Right lower quadrant	229 (51.6)	237 (53.0)
Whole abdomen	63 (14.2)	69 (15.4)
Epigastric	48 (10.8)	49 (11.0)
Lower abdomen	37 (8.3)	27 (6.0)
Periumbilical	25 (5.6)	31 (6.9)
Right abdomen	14 (3.2)	16 (3.6)
Other	10 (2.3)	6 (1.3)
Not applicable‡	18 (4.1)	12 (2.7)

Table 1. (Continued.)

Characteristic	Low-Dose CT Group (N=444)	Standard-Dose CT Group (N=447)
Body temperature — °C		
Median	36.8	36.7
Interquartile range	36.4–37.2	36.5–37.1
Blood-test results		
White-cell count — $1 \times 10^3 / \text{mm}^3$		
Median	10.7	10.8
Interquartile range	7.8–14.1	8.0–14.3
Segmented neutrophils — %		
Median	77.0	77.3
Interquartile range	65.8–85.2	65.5–83.9
C-reactive protein — mg/dl		
Median	0.5	0.7
Interquartile range	0.3–2.5	0.3–3.3
Type of CT scanner — no. (%)		
16-detector-row	177 (39.9)	191 (42.7)
64-detector-row	154 (34.7)	144 (32.2)
256-detector-row	113 (25.5)	112 (25.1)
Radiologist — no. (%)		
Expert	217 (48.9)	225 (50.3)
Nonexpert	227 (51.1)	222 (49.7)

* There were no significant differences between the two groups in any of the baseline characteristics.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡ The presence of pain was not formally documented in the medical record.

the 12 negative appendectomies are provided in the Supplementary Appendix.) The appendiceal perforation rate was 26.5% (44 of 166 patients) in the low-dose CT group and 23.3% (42 of 180 patients) in the standard-dose CT group ($P=0.46$).

DIAGNOSTIC PERFORMANCE OF CT AND DIAGNOSTIC CONFIDENCE

For 5 patients in the low-dose CT group and 1 patient in the standard-dose CT group, the CT reports were not prepared according to the predefined structured format. The remaining 433 patients in the low-dose CT group and 440 in the standard-dose CT group were included in the final analyses of the CT reports (Table 4). For the diagnosis of appendicitis, the low-dose CT group did not differ significantly from the standard-dose CT group with respect to the AUC (0.970 and 0.975, respectively; $P=0.69$), although diagnostic confidence tended to be more compromised in the low-dose CT group than in the standard-dose CT group.

(The data reported by the expert and nonexpert radiologists are provided in the Supplementary Appendix.)

DISCUSSION

In this study, the low-dose CT group was noninferior to the standard-dose CT group with regard to negative appendectomy rates. Neither the appendiceal perforation rate nor the diagnostic performance of CT for appendicitis differed significantly between the two groups. Although we used an intention-to-treat analysis, a per-protocol analysis would have shown the same results, since all the patients who were included in the analysis remained in the groups to which they were originally assigned. The point estimate for the difference in negative appendectomy rates between the two groups (0.3 percentage points) suggests that the use of low-dose CT instead of standard-dose CT in an estimated 330 patients would result in

Table 2. Clinical Outcomes.*

Outcome	Low-Dose CT Group	Standard-Dose CT Group	P Value†	Difference (95% CI)	Risk Ratio (95% CI)
<i>percentage points</i>					
Primary end point					
Negative appendectomy rate — no. of patients/total no. (%)	6/172 (3.5)	6/186 (3.2)		0.3 (–3.8 to 4.6)	1.08 (0.37 to 3.13)
Secondary end points					
Need for one or more additional imaging tests — no. of patients/total no. (%)	14/438 (3.2)	7/441 (1.6)	0.09	1.6 (–0.4 to 3.9)	2.01 (0.84 to 4.81)
Interval between CT and nonincidental appendectomy — hr‡			0.02		
Median	7.1	5.6			
Interquartile range	4.3 to 11.7	3.4 to 9.2			
Interval between CT and discharge without surgery — hr			0.63		
Median	2.5	2.4			
Interquartile range	1.5 to 4.2	1.4 to 4.4			
Appendiceal perforation rate — no. of patients/total no. (%)	44/166 (26.5)§	42/180 (23.3)¶	0.46	3.2 (–5.9 to 12.4)	1.14 (0.79 to 1.64)
Hospital stay associated with nonincidental appendectomy — days			0.54		
Median	3.4	3.2			
Interquartile range	2.7 to 4.1	2.5 to 4.1			

* A total of 12 patients who were lost to follow-up (6 in each group) were excluded from the analysis. CI denotes confidence interval.

† The P values were calculated with the use of Fisher's exact test or the Mann–Whitney U test, as appropriate.

‡ Data do not include 3 patients who underwent delayed appendectomy after percutaneous drainage of an abscess.

§ In the low-dose CT group, 36 cases of perforation were identified during the operation, and an additional 8 were revealed on microscopical examination of the appendectomy specimens.

¶ In the standard-dose CT group, 30 cases of perforation were identified during the operation, and an additional 12 were revealed on microscopical examination of the appendectomy specimens.

one additional negative appendectomy. This can be weighed against the potentially higher incidence of cancer resulting from the use of standard-dose as opposed to low-dose CT (see the Supplementary Appendix); this incidence can be estimated according to a method used in previous studies.^{14,28,29} However, it is highly debatable whether the radiation levels used in our two groups can actually induce cancer and whether use of the low dose instead of the standard dose can actually reduce the carcinogenic risk. Nonetheless, to ensure patient safety, it would be prudent to assume that both statements are true on the basis of the linear no-threshold approach.³⁰ Although the appropriateness of this approach is debated, it is used most frequently for judging radiation effects.

During the past decade, there has been a surge in the use of CT for diagnosing appendicitis in

the United States,^{4–10} with more than 250,000 appendectomies performed in patients each year.¹² The majority of these patients undergo preoperative CT,^{5,7–10} and there are many more patients for whom the results on CT examination are negative. A similar trend exists in Korea, where this study was conducted, although no such data have been published. Such a large number of exposures may ultimately have an effect on the incidence of cancer in these populations, although the individual risk for cancer induced by a CT examination is extremely low.

Our findings corroborate those of previous exploratory studies that support a reduction in the radiation dose when CT is used in the diagnosis of appendicitis.^{15–17} These results can be attributed to the excellent imaging capability of modern CT scanners and the intrinsic simplicity of CT-image

interpretation in diagnosing appendicitis, which may offset the loss in image quality due to low-dose CT techniques.¹⁸ The dose of radiation currently used reflects historical data, being without scientific basis,³¹ and varies widely among hospitals (from 160 to 280 mA·sec in terms of the x-ray tube current-time product).³² Furthermore, although there is no reason to use the same dose in young patients with appendicitis as in elderly patients with malignant lesions, attempts have rarely been made to differentiate the dose level according to application.¹⁶

The patients in the low-dose CT group, as compared with those in the standard-dose CT group, were more likely to require additional imaging tests and had a longer interval between the CT examination and appendectomy, which may represent the referring physicians' hesitation to base their decisions on the low-dose CT findings. As compared with standard-dose CT, low-dose CT was also limited in terms of the diagnostic confidence for appendicitis and the diagnosis of appendiceal perforation. Overall, our results indicate that low-dose CT, despite its limitations, may be used instead of standard-dose CT as the first-line imaging test, because the ultimate clinical outcomes and diagnostic performance can be maintained if low-dose CT is incorporated into the diagnostic process with selective additional imaging and clinical observation.

In terms of alternative diagnoses, our results are not conclusive. In general, young adults whose presentations mimic appendicitis would rarely prove to have a serious chronic or malignant disease. Reports indicate that it is feasible to reduce the dose of CT radiation considerably for diagnosing urinary stones³³ or colonic diverticulitis,³⁴ which are important alternative diagnoses. For other alternative diagnoses, such as complicated adnexal cyst, pelvic inflammatory disease, or acute pyelonephritis, CT examination may not be critical, since in these cases the diagnosis should be based on clinical findings or other types of diagnostic tests.

The broad eligibility criteria used in this study, which depended largely on the judgment of individual emergency department physicians, may have led to some heterogeneity among the patients who were included. Such heterogeneity with respect to the initial clinical suspicion³⁵ and referral for CT examination³⁶ reflects the reality of clinical practice and is inevitable, since none of the combinations of symptoms and signs are considered

Table 3. Negative Appendectomies.*

Characteristic	Negative Appendectomy	
	Low-Dose CT Group	Standard-Dose CT Group
	<i>number/total number</i>	
Total	6/172	6/186
Sex		
Female	5/90	2/83
Male	1/82	4/103
Body-mass index		
<18.5 (underweight)	0/20	1/19
18.5–24.9 (normal)	5/119	4/129
25.0–29.9 (overweight)	0/32	1/33
30.0–34.9 (class I obesity)	1/1	0/4
35.0–39.9 (class II obesity)	0/0	0/1
≥40.0 (class III obesity)	0/0	0/0
Type of CT scanner		
16-detector-row	3/58	2/73
64-detector-row	1/73	2/64
256-detector-row	2/41	2/49
Radiologist		
Expert	1/81	2/91
Nonexpert	5/91	4/95
Appendectomy approach		
Laparoscopic	6/109	4/115
Open	0/63	2/71

* The sex distribution for negative appendectomies differed between the low-dose and standard-dose CT groups ($P=0.13$); also, negative appendectomies tended to be more frequent in both the low-dose group ($P=0.13$) and the standard-dose group ($P=0.45$) when the CT scan was interpreted by a non-expert radiologist, as compared with an expert radiologist, and in the low-dose CT group in cases of laparoscopic appendectomy ($P=0.05$). Owing to the limited number of negative appendectomies in this study, a formal subgroup analysis was not performed.

reasonably accurate or reliable for establishing the diagnosis of appendicitis.³⁷⁻³⁹ The prevalence of confirmed appendicitis in our study, which is related to the pretest probability and CT-utilization pattern, was approximately 40% in both the low-dose and the standard-dose CT groups, as compared with rates of 39%⁹ and 24%⁴⁰ reported in two large, cross-sectional studies.

This study had certain limitations. First, the study setting may have been biased toward low-dose CT, since the investigators who were experienced in and favorably disposed toward low-dose CT (including the expert radiologists) played a major role in caring for the patients. Second, the

Table 4. Diagnostic Performance of CT and Diagnostic Confidence.*

CT Result	Low-Dose CT Group (N=433)	Standard-Dose CT Group (N=440)	Difference (95% CI)†	P Value‡
Diagnosis of appendicitis				
AUC	0.970	0.975	-0.005 (-0.030 to 0.020)	0.69
Sensitivity — no. of patients/total no. (%)§	156/165 (94.5)	171/180 (95.0)	-0.5 (-5.6 to 4.5)	>0.99
Specificity — no. of patients/total no. (%)§	250/268 (93.3)	244/260 (93.8)	-0.6 (-4.9 to 3.8)	0.72
Likelihood of appendicitis — no. of patients/total no. (%)¶				
Diagnosis subsequently confirmed				0.03
Grade 1	2/165 (1.2)	4/180 (2.2)		
Grade 2	7/165 (4.2)	5/180 (2.8)		
Grade 3	13/165 (7.9)	11/180 (6.1)		
Grade 4	53/165 (32.1)	34/180 (18.9)		
Grade 5	90/165 (54.5)	126/180 (70.0)		
Diagnosis subsequently not confirmed				0.06
Grade 1	185/268 (69.0)	206/260 (79.2)		
Grade 2	65/268 (24.3)	38/260 (14.6)		
Grade 3	11/268 (4.1)	11/260 (4.2)		
Grade 4	3/268 (1.1)	3/260 (1.2)		
Grade 5	4/268 (1.5)	2/260 (0.8)		
Indeterminate interpretation, grade 3 — no. of patients/total no. (%)	24/433 (5.5)	22/440 (5.0)	0.5 (-2.5 to 3.6)	0.66
Diagnosis of appendiceal perforation				
Sensitivity — no. of patients/total no. (%)	16/44 (36.4)	23/42 (54.8)	-18.4 (-38.0 to 2.8)	0.09
Specificity — no. of patients/total no. (%)	110/121 (90.9)	121/138 (87.7)	3.2 (-4.6 to 11.0)	0.33

* The 12 patients who were lost to follow-up (6 in each group) were excluded from the analysis. An additional 6 patients (5 in the low-dose CT group and 1 in the standard-dose CT group) were excluded from the analysis since the data were classified as missing because the CT report did not conform to the structured format. AUC denotes area under the receiver-operating-characteristic curve.

† With the exception of the AUC, values for the difference between the two groups are percentage points.

‡ All P values were calculated with the use of the nonparametric Wilcoxon statistic or Fisher's exact test, as appropriate.

§ A grade of 3 or higher was considered to be positive for the diagnosis.

¶ Grade 1 denotes appendicitis definitely absent; grade 2, appendicitis probably absent; grade 3, indeterminate for the presence of appendicitis; grade 4, appendicitis probably present; and grade 5, appendicitis definitely present. (For further details, see the Supplementary Appendix.)

study was not sufficiently powered to conclusively analyze the potential effects of patient-related or radiologist-related factors on negative appendectomy rates or any differences in these effects between the low-dose and standard-dose CT groups. Third, few of the patients included in our study were obese. When these limitations are considered, the generalizability of the results to patients with a large body habitus and radiologists with varying levels of expertise may need to be confirmed. In addition, our study may have been subject to biases that would potentially inflate the diagnostic performance of the CT reports,¹ since pathological verification of appendicitis was made

selectively in patients with positive CT results and the assessors who interpreted the reference standard were aware of the preoperative CT results.

In conclusion, we found that the use of low-dose CT as the first-line imaging test was non-inferior to standard-dose CT with respect to the negative appendectomy rate among young adults with suspected appendicitis.

Supported by a grant (OM-09-01) from GE Healthcare Medical Diagnostics, Korea; a Mid-Career Researcher Program grant (2011-0012117) from the National Research Foundation of Korea; and a grant (04-2011-004) from the Seoul National University Bundang Hospital Research Fund. No potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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