CW-06 Randomized controlled trial in radiology research

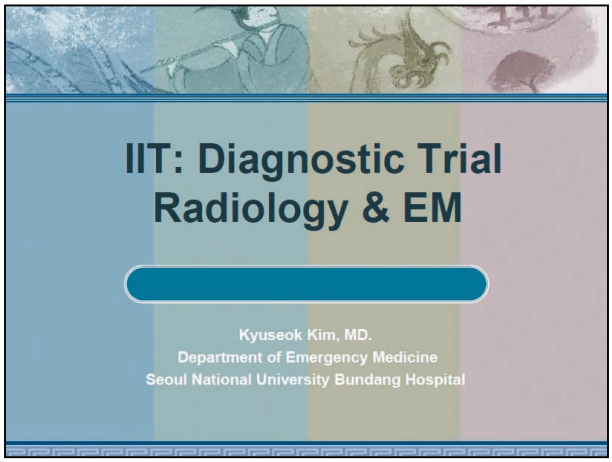
15:50-16:20 201

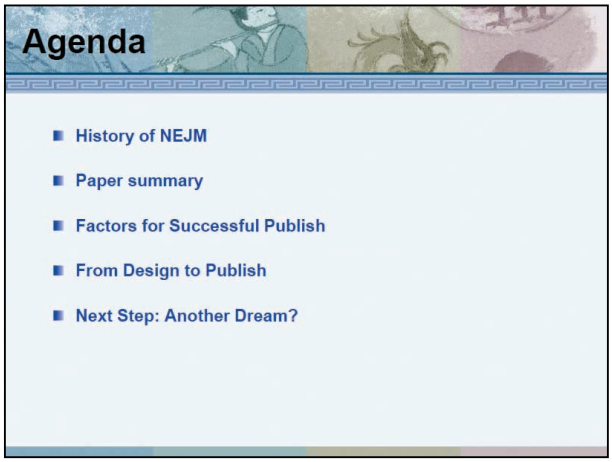
Chairperson(s): Jeong Min Lee *Seoul National University Hospital, Korea*

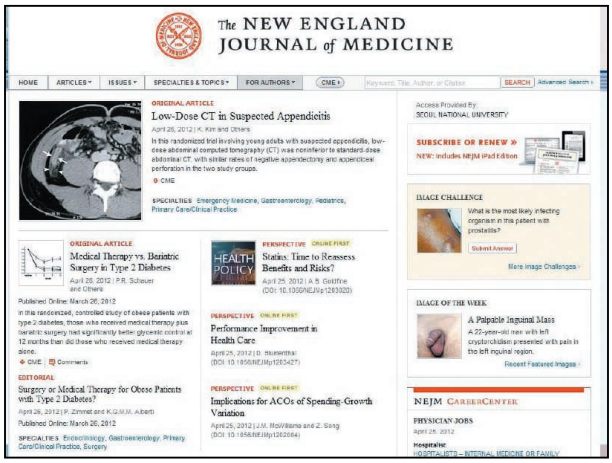
연구자 주도 단기관 diagnostic trial의 예: 영상의학과 – 응급의학과 협력연구

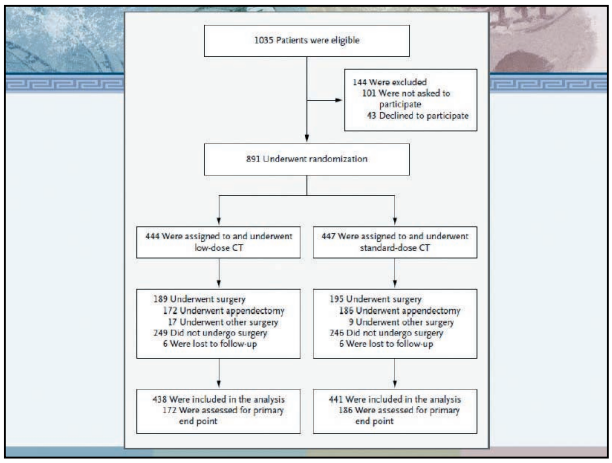
Kyuseok Kim

Seoul National University Bundang Hospital, Korea. dremkks@snubh.org









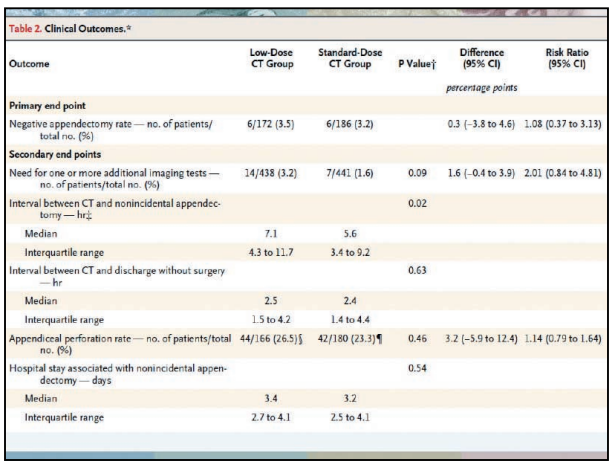


Table 2. Clinical Outcomes.*

Outcome	Low-Dose CT Group	Standard-Dose CT Group	P Value†	Difference (95% CI)	Risk Ratio (95% CI)
				percentage points	
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			

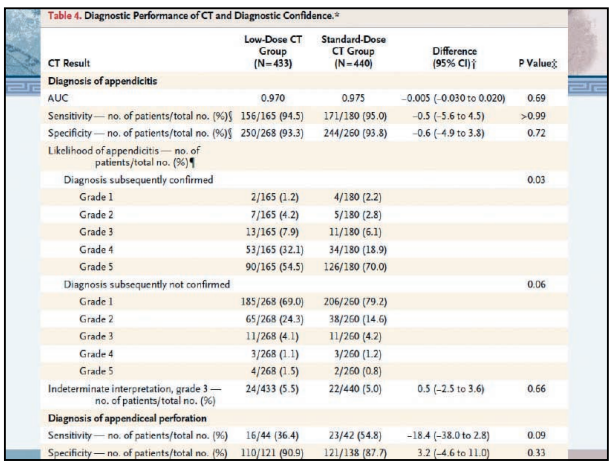
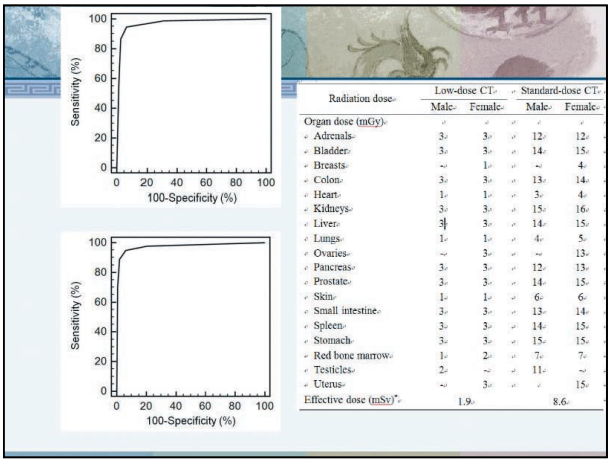
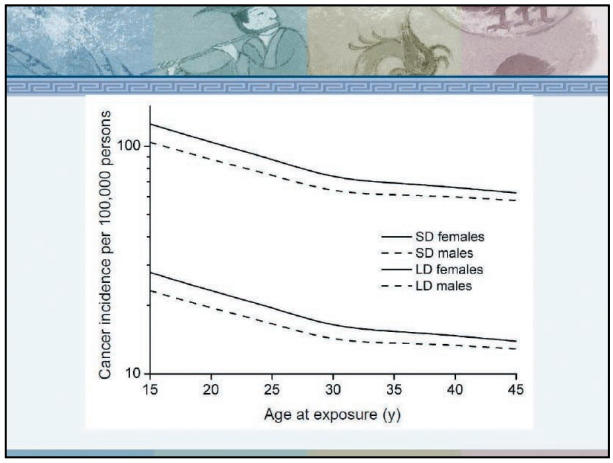


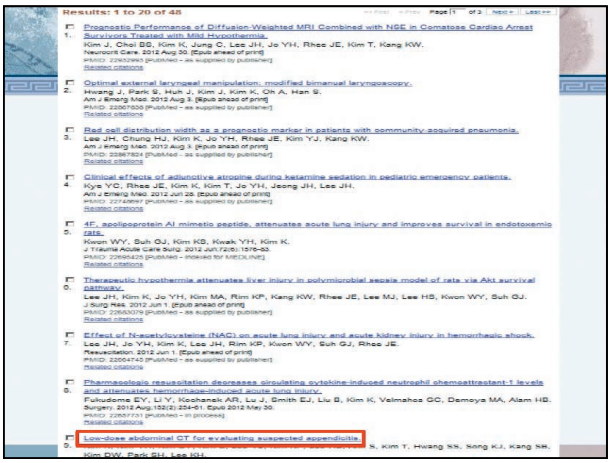
Table 4. Diagnostic Performance of CT and Diagnostic Confidence.*

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



Radiation dose	Low-dose CT		Standard-dose CT	
	Male	Female	Male	Female
Organ dose (mGy)				
Adrenals	3	3	12	12
Bladder	3	3	14	15
Breasts	–	1	–	4
Colon	3	3	13	14
Heart	1	1	3	4
Kidneys	3	3	15	16
Liver	3	3	14	15
Lungs	1	1	4	5
Ovaries	–	3	–	13
Pancreas	3	3	12	13
Prostate	3	3	14	15
Skin	1	1	6	6
Small intestine	3	3	13	14
Spleen	3	3	14	15
Stomach	3	3	15	15
Red bone marrow	1	2	7	7
Testicles	2	–	11	–
Uterus	–	3	–	15
Effective dose (mSv)*	1.9		8.6	





Factors for Successful Publish

- Good Luck!
- Have an Impossible Dream!
- Being prepared!
- Cooperation!

Factors for Successful Publish: Being Prepared

- 2000…
  - CT for appendicitis: Blame…
- Pubmed
- 2002-2003: 수도병원
- 2004: Retrospective study
- 2005: Prospective study
- 2006: Another Prospective study
- Sliding Slab

THE IMPACT OF HELICAL COMPUTED TOMOGRAPHY ON THE NEGATIVE APPENDECTOMY RATE: A MULTI-CENTER COMPARISON

Kyuseok Kim, MD,* Christopher C. Lee, MD,† Kyoung-Jun Song, MD,‡ Woojeong Kim, MD,§ Gil|oon Suh, MD,‖ and Adam J. Singer, MD†

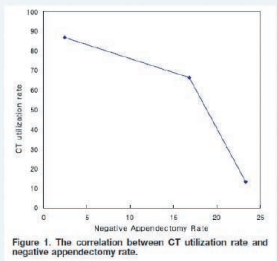
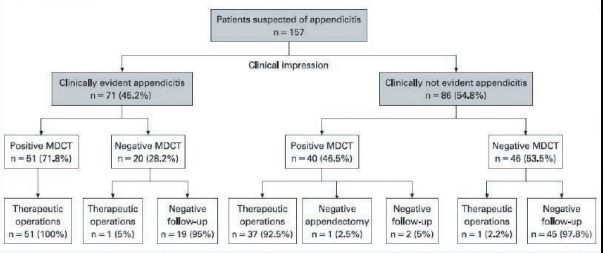


Figure 1. The correlation between CT utilization rate and negative appendectomy rate.

EMJ ONLINE

Impact of helical computed tomography in clinically evident appendicitis



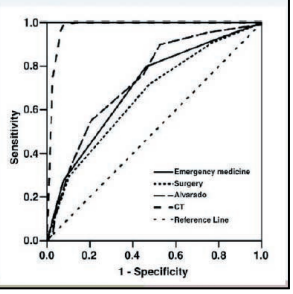
→Need scoring system

The accuracy of emergency medicine and surgical residents in the diagnosis of acute appendicitis

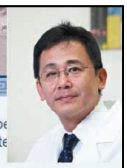
You Hwan Jo MD[a], Kyuseok Kim MD, PhD[a,*], Joong Eui Rhee MD[a], Tae Yun Kim MD[a], Jin Hee Lee MD[a], Sung-Bum Kang MD[b], Duck-Woo Kim MD[b], Young Hoon Kim MD[c], Kyoung Ho Lee MD[c], So Yeon Kim MD[c], Christopher C. Lee MD[d], Adam J. Singer MD[d]

Table 3 Comparison of diagnostic accuracy between emergency medicine and SRs

Group	EM (N = 191)	Surgery (N = 191)	P
1	30/37 (81.1)	32/41 (78.1)	.740
2	59/89 (66.3)	47/76 (61.8)	.553
3	14/41 (34.2)	22/45 (48.9)	.161
4	8/24 (33.3)	10/29 (34.5)	.930



Dr Lee's aspect



- Joo S-M, Lee KH, Kim YH, et al. Detection of the normal appe low-dose unenhanced CT: use of the sliding slab averaging te Radiology 2009;251:780-7.
- Kim SY, Lee KH, Kim K, et al. Acute appendicitis in young adults: low- versus standard-radiation-dose contrast-enhanced abdominal CT for diagnosis. Radiology 2011;260:437-45.
- Lee KH, Kim YH, Hahn S, et al. Computed tomography diagnosis of acute appendicitis: advantages of reviewing thin-section datasets using sliding slab average intensity projection technique. Invest Radiol 2006;41:579-85.
- Lee KH, Lee HS, Park SH, et al. Appendiceal diverticulitis: diagnosis and differentiation from usual acute appendicitis using computed tomography. J Comput Assist Tomogr 2007;31:763-9.
- Seo H, Lee KH, Kim HJ, et al. Diagnosis of acute appendicitis with sliding slab ray-sum interpretation of low-dose unenhanced CT and standard-dose intravenous contrast-enhanced CT scans. Am J Roentgenol 2009;193:96-105.

Start…

- Phone Call from Dr Lee: late 2008
- Meeting at Fitness club
- Low dose CT
- Before-After study
  - Low dose vs. Standard dose
  - Surrogate outcome: Test characteristics, AUC
- RCT
  - Clinical outcome: Negative appendectomy, perforation

Cooperation…

- Need Good people
  - Radiologist
  - Surgeon, pathologist
  - Statistician
  - CRC

- Statistical Father of mine!

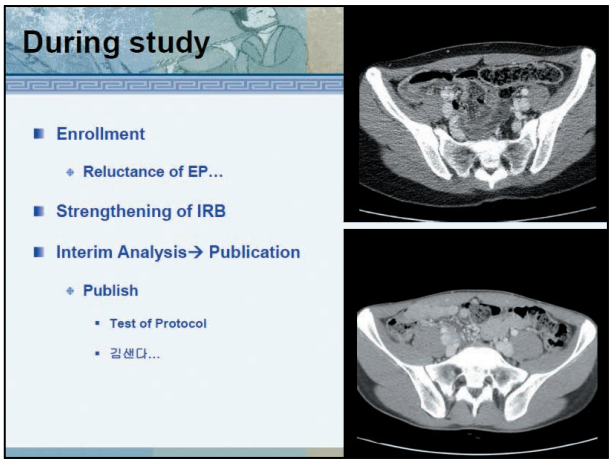

직장암 복강경 수술
안전성 입증
- 외과 강성범 교수팀 세계 최초 규명
란센 종양학(Lancet oncology) 게재
THE LANCET Oncology
Morbidity and Mortality of Laparoscopic Gastrectomy Versus Open Gastrectomy for Gastric Cancer
An Interim Report—A Phase III Multicenter, Prospective, Randomized Trial (KLASS Trial)


선수 중의 선수…
ROC curve에 대한 Review논문을
영어로 쓴 사람
Radiology Associate editor
김규석은?
그거보고 공부한 사람…


Meeting…
Primary outcome
Clinical vs. Surrogate
Sensitivity, specificity, PPV, NPV, AUC
NAR vs. Perforation rate
Design: Non-inferior trial
Sample Size
Funding


Factors for Successful Publish:
Sabbatical leave
Study
Preparation: Nov 2008- Aug 2009
Enroll: Sep 2009-Jan 2011
Dr. Kim: Aug 2009- Aug 2010
Dr. Lee: Jan 2010- Jan 2011
Bunch of time to study!!!
Communication: 070전화…
Prof Kim from Nuclear Engineering


CT 방사선: 암발생률
Berrington de Gonzalez A, Kim KP, Smith-Bindman R
D. Myocardial perfusion scans: projected population c
from current levels of use in the United States. Circula
2010;122:2403-10.
Berrington de Gonzalez A, Mahesh M, Kim KP, et al.
cancer risks from computed tomographic scans perfo
United States in 2007. Archives of internal medicine
2009;169:2071-7.
Kim KP, Einstein AJ, Berrington de Gonzalez A. Coronary artery calcification screening: estimated radiation dose and cancer risk. Archives of internal medicine 2009;169:1188-94.
Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet 2012.
Smith-Bindman R, Lipson J, Marcus R, et al. Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. Archives of internal medicine 2009;169:2078-86.


During study
Enrollment
Reluctance of EP…
Strengthening of IRB
Interim Analysis→ Publication
Publish
Test of Protocol
김샘다…

Preparing Manuscript

- Target
  - Annals of Internal Medicine
  - NEJM, JAMA, Lancet…
- 6 months
- Open Discussion between Inter-Department
- Hot Discussion: Arguing vs. Fighting
  - Serious Adverse Event
  - Number of EP, Surgeon…
  - Etc…

Revision

- 5 peer reviewer (4+1 statistical reviewer)
- 10 pages (20 pages with double space)
- Dr. Lee & Dr. Park
- 1.5 months…

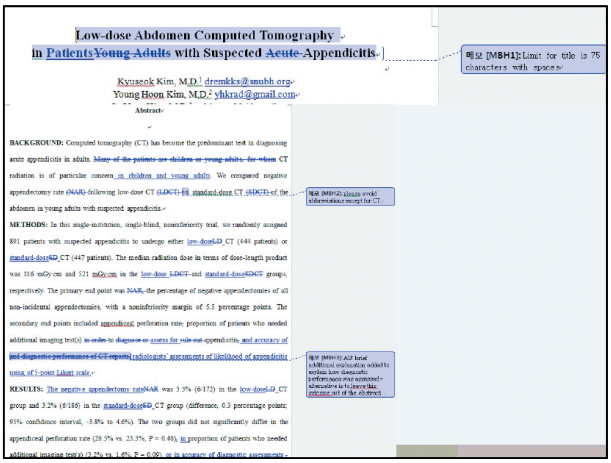
2nd Revision

From: <editorial@nejm.org>
Date: Wed Jan 4, 2012 at 1:56 AM
Subject: New England Journal of Medicine 11-10734.R1
To: kholeemail@gmail.com

Dear Dr. Lee:

We are pleased to inform you that we remain interested in your manuscript, "Low-Dose Abdomen CT in Young Adults with Suspected Acute Appendicitis." Before we can accept it, we ask that you address the additional suggestions and questions highlighted in the attached version of your paper.

Your revised paper should not exceed 2700 words for text, 250 words for abstract, and 75 characters with spaces for title. In the event that your manuscript is accepted, it must fit within no more than 10 printed pages. Additional shortening is sometimes necessary during the production process.


Low-dose Abdomen Computed Tomography in Patients Young Adults with Suspected Acute Appendicitis.

Kyuseok Kim, M.D.[1] dremkks@snubh.org
Young Hoon Kim, M.D.[2] yhkrad@gmail.com

Abstract

BACKGROUND: Computed tomography (CT) has become the predominant test in diagnosing acute appendicitis in adults. Many of the patients are children or young adults, for whom CT radiation is of particular concern. In children and young adults. We compared negative appendectomy rate (NAR) following low-dose CT (LDCT) to standard-dose CT (SDCT) of the abdomen in young adults with suspected appendicitis.

METHODS: In this single-institution, single-blind, noninferiority trial, we randomly assigned 891 patients with suspected appendicitis to undergo either low-dose LD CT (444 patients) or standard-dose SD CT (447 patients). The median radiation dose in terms of dose-length product was 116 mGy·cm and 521 mGy·cm in the low-dose LDCT and standard-dose SDCT groups, respectively. The primary end point was NAR, the percentage of negative appendectomies of all non-incidental appendectomies, with a noninferiority margin of 5.5 percentage points. The secondary end points included appendiceal perforation rate, proportion of patients who needed additional imaging test(s) in order to diagnose or assess for rule out appendicitis, and accuracy of and diagnostic performance of CT reports radiologists' assessments of likelihood of appendicitis using of 5-point Likert scale.

RESULTS: The negative appendectomy rateNAR was 3.5% (6/172) in the low-dose LD CT group and 3.2% (6/186) in the standard-dose SD CT group (difference, 0.3 percentage points; 95% confidence interval, -3.8% to 4.6%). The two groups did not significantly differ in the appendiceal perforation rate (26.5% vs. 23.3%, P = 0.46), in proportion of patients who needed additional imaging test 0 (3.2% vs. 1.6%, P = 0.05), or in accuracy of diagnostic assessments.

Acceptance

2012.1.28. 05:19

New England Journal of Medicine 11-10734.R2

editorial@nejm.org
dremkks, yhkrad, sykimsnubh, flora.snuh, yoonjin319, kpkim, klight, hye2, ahnsoyeon, emkity, cyb

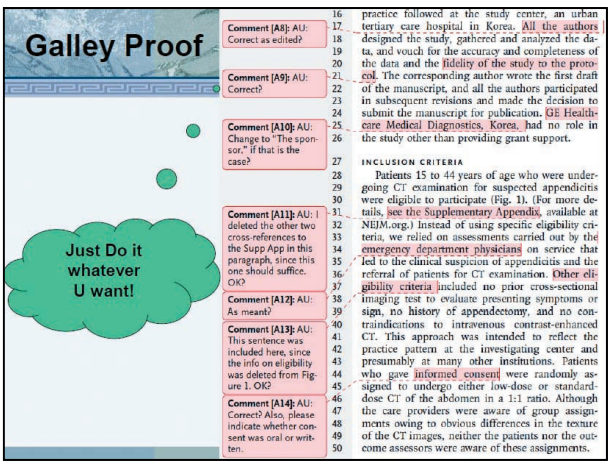
Dear Dr. Lee and co-authors,

Thank you for the article, "Low-dose Abdomen Computed Tomography for Evaluating Suspected Appendicitis," which the Journal is pleased to accept for publication.

This acceptance is made with the understanding that neither the article itself nor any part of its essential substance, tables or figures has been published or will be submitted for publication elsewhere before it appears in the Journal. The acceptance is also made with the understanding that all the authors, the data, and its presentation meet the requirements as described in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (www.icmje.org).

Please note that the acceptance of your manuscript should be considered confidential information to be shared only with your coauthors until its final publication. To ensure that no news reports about the article appear prematurely in any form, do not speak to the media, hold press conferences, or issue news releases about your paper before the week of publication. You must receive an explicit commitment to withhold release of the information until the embargo is lifted at 5:00 p.m. (Eastern Time in the United States) on the day before the date of publication. If there are any questions about this policy, you should discuss them with the Editor.

Galley Proof


Comment [A8]: AU: Correct as edited?

Comment [A9]: AU: Correct?

Comment [A10]: AU: Change to "The sponsor," if that is the case?

Comment [A11]: AU: I deleted the other two cross-references to the Supp App in this paragraph, since this one should suffice. OK?

Comment [A12]: AU: As meant?

Comment [A13]: AU: This sentence was included here, since the info on eligibility was deleted from Figure 1. OK?

Comment [A14]: AU: Correct? Also, please indicate whether consent was oral or written.

Just Do it whatever U want!

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

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. Other eligibility criteria included no prior cross-sectional imaging test to evaluate presenting symptoms or sign, no history of appendectomy, and no contraindications to intravenous contrast-enhanced CT. This approach was intended to reflect the practice pattern at the investigating center and presumably at many other institutions. Patients who gave 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.

분당서울대병원 김규석·이경호 교수팀

맹장염 진단 저선량CT 유용성 입증

〈방사선량 일반CT의 25% 수준〉

분당서울대병원은 응급의학과 김규석(왼쪽 사진), 영상의학과 이경호(오른쪽) 교수팀이 기존 일반CT 대비 25% 수준의 방사선만 쓰는 저선량CT가 충수돌기염 진단에 유용하다는 연구결과를 세계 최고 권위의 학술지 '뉴 잉글랜드 저널 오브 메디슨(NEJM)' 최신호에 게재했다고 26일 밝혔다.

흔히 맹장염이라 불리는 충수돌기염은 맹장 끝에 붙어있는 충수에 생기는 염증 질환으로 자칫 진단이 늦어지면 복막염으로 발전, 생명을 위협하게 된다. 일반CT 검사는 이 같은 합병증 발생 위험을 막고 충수돌기염의 조기 발견에 큰 도움이 되지만 방사선 노출에 의한 발암 위험성이 문제점으로 지적된다. 저선량CT는 이를 방지할 목적으로 최근 활발히 사용되는 방사선 검사 장비다. 일반적으로 CT 촬영 시 방사선량을 낮추면 영상 화질이 떨어져 진단에 어려움이 따른다.

김 교수팀은 2009년 9월부터 2011년 1월까지 충수돌기염 의심 환자 891명을 약 절반씩 나눠 진단효과 면에서 두 장비 간에 차이가 있는지를 비교, 검증했다. 그 결과 저선량CT 군의 오판율(충수돌기염 의증으로 진단됐으나 수술 후 염증이 없다고 판명된 비율)은 3.5%로 일반CT 군의 3.2%와 큰 차이가 없는 것으로 나타났다.

김 교수는 "NEJM이 이 논문을 채택한 것은 CT 검사 시 발암 논란이 있는 방사선 노출 위험을 줄이려는 의학계의 공통 관심사가 반영된 결과로 보인다"며 "충수돌기염 진단에서 저선량CT의 유용성이 입증됨에 따라 앞으로 저선량CT가 충수돌기염 진단검사의 표준 방법으로 자리 잡을 가능성이 높아졌다"고 말했다.

이기수 의학전문기자 kslee@kmib.co.kr

방사선 노출 적은 '저선량 CT'

"맹장염 진단 가능" 유용성 입증

분당서울대병원

김규석 교수 이경호 교수

방사선 노출이 적은 저선량 컴퓨터단층촬영(CT)으로도 충수돌기염(맹장염) 진단이 잘 되는 것으로 나타났다. 방사선 노출에 의한 발암위험 불안도 크게 낮출 것으로 보인다.

분당서울대병원 응급의학과 김규석·영상의학과 이경호 교수팀은 충수돌기염 진단에 방사선량을 4분의 1로 줄인 저선량 CT로 진단한 유용성을 입증해 뉴잉글랜드 저널 오브 메디슨(NEJM IF=53.5) 최신호에 게재됐다고 26일 밝혔다.

교수팀은 지난 2009년 9월부터 2011년 1월까지 충수돌기염 진단을 위해 CT 검사가 필요했던 15~44세 환자 891명을 대상으로 무작위 대조 비교임상시험을 실시했다.

그 결과, 충수돌기염이 의심돼 수술 후 결국 염증이 없다고 판명된 비율은 저선량 CT군이 3.5%, 일반 CT군은 3.2%로 차이가 없었다. 또 충수돌기 천공률(중증도 평가)도 저선량 CT군은 26.5%, 일반 CT군은 23.3%로 비슷했다.

충수돌기염은 맹장 끝에 붙어있는 충수 돌기에 발생하는 염증으로 우리나라에서만 매년 9만5000여명이 수술을 받을 정도로 흔한 질환이다.

충수돌기염의 경우 비교적 간단히 수술을 통해 치료할 수 있지만 증상이 모호해 정확한 진단이 어려운 경우가 있다.

또 수술이 지연되면 충수가 터지는 등 합병증이 발생할 확률이 커져 초기에 정확하고 빠르게 진단을 내리는 것이 중요하다.

하지만 CT 사용으로 충수돌기염을 포함한 다양한 질병에 대한 빠르고 정확한 진단은 가능해졌으나 CT 촬영 시 방사선 노출에 의한 발암위험도 증가가 문제다.

김 교수는 "충수돌기염에서 저선량 CT의 유용성을 입증함에 따라 충수돌기염 진단에 저선량 CT를 이용하는 것이 표준 방법으로 자리 잡는데 중요한 근거가 될 것"이라고 말했다.

정명진 의학전문기자