Journal Club

Uncomplicated appendicitisに対する治療

抗菌薬？手術？？
その判断基準は？？？

千里救命救急センター
橘高　弘忠

PubMed.gov

acue appendicitis

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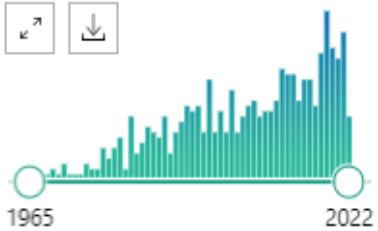

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- [ ] Associated data

ARTICLE TYPE

- [ ] Books and Documents
- [ ] Clinical Trial
- [ ] Meta-Analysis
- [x] Randomized Controlled Trial

Filters applied: Randomized Controlled Trial. Clear all

Showing results for *acute appendicitis*

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1 Cite Share

Topical antibiotic therapy in **acute appendicitis**.

Stoller JL.

Br J Clin Pract. 1965 Dec;19(12):687-8.

PMID: 5323325 Clinical Trial. No abstract available.

2 Cite Share

Topical ampicillin in the appendicectomy wound: report of double-blind trial.

Rickett JW, Jackson BT.

Br Med J. 1969 Oct 25;4(5677):206-7. doi: 10.1136/bmj.4.5677.206.

PMID: 4900147 Free PMC article. Clinical Trial.

3 Cite Share

Simulation of clinical diagnosis: a comparative study.

De Dombal FT, Horrocks JC, Staniland JR, Gill PW.

Br Med J. 1971 Jun 5;2(5761):575-7. doi: 10.1136/bmj.2.5761.575.

PMID: 5579197 Free PMC article. Clinical Trial.

4 Cite

Peritoneal drainage and systemic antibiotics after appendicectomy. A prospective trial.

Magarey CJ, Chant AD, Rickford CR, Margarey JR.

Uncomplicated appendicitis

- 急性虫垂炎は、膿瘍形成や穿孔を伴うcomplicated appendicitis とそれらを伴わないuncomplicated appendicitis の2つに大別される

- Uncomplicated appendicitisでは、複数のRCTで抗菌薬治療の有用性が示されている

- 一方、抗菌薬治療開始した後、手術移行を予測する因子は不明

本日の論文

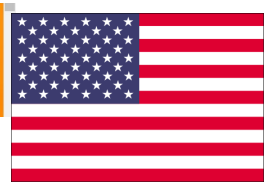
糞石(+)を含む単純性虫垂炎に対する
抗菌薬群vs.手術群のRCT（CODA trial）

N Eng J Med. 2020 Nov 12;383(20):1907-1919.

抗菌薬治療開始後30日以内に手術移行する
リスク因子を検証（CODA trialの2次解析）

AMA Surg. 2022 Mar 1;157(3):e216900.

急性虫垂炎に対する治療法の歴史



Acute Appendicitis: *

An Analysis of 1,662 Consecutive Cases

J. Reed Babcock, M.D., F.A.C.S., William Mark McKinley, M.D.

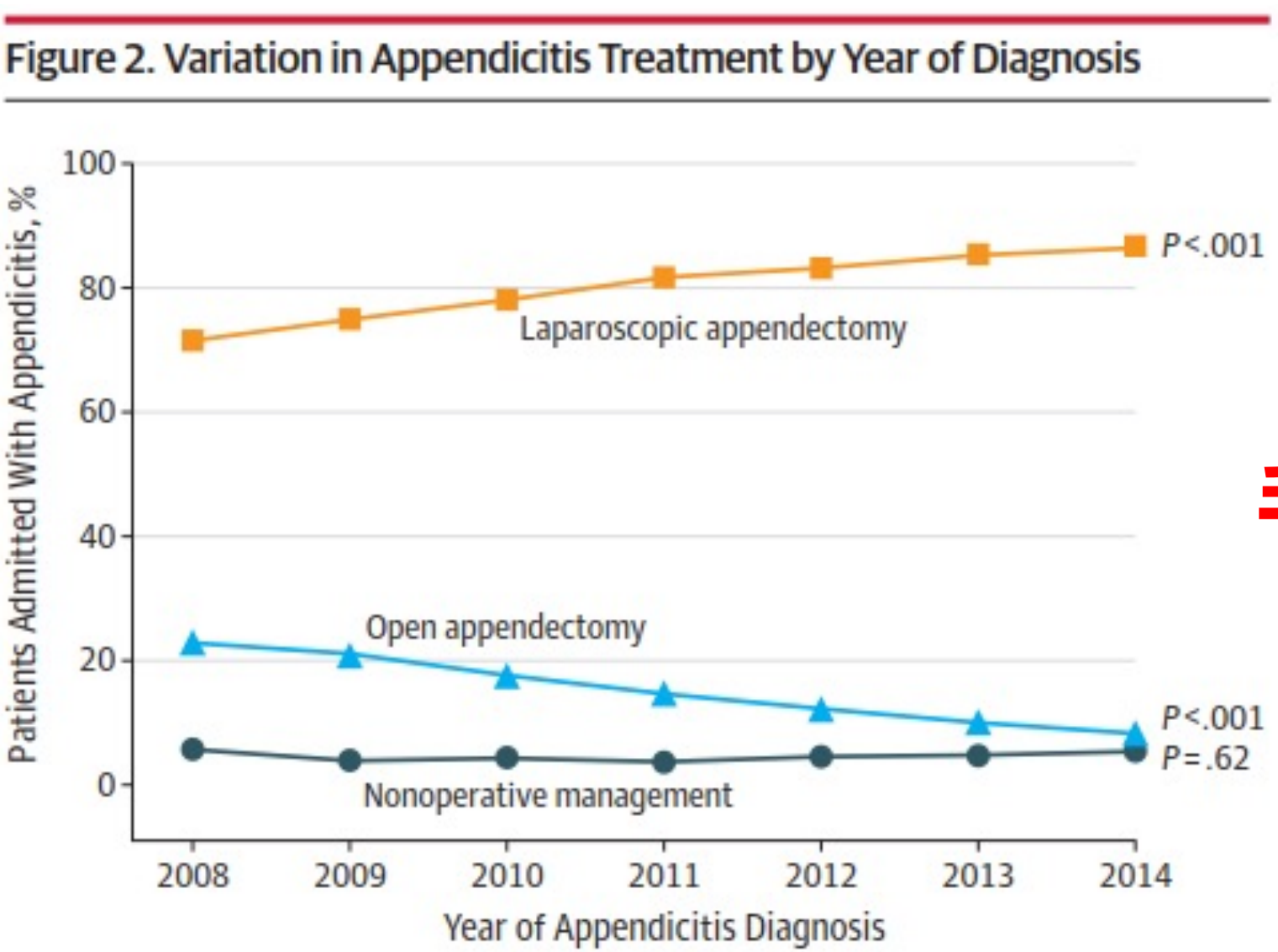
Danville, Pennsylvania

Ann Surg. 1959 150(1).131-41

From the beginning of this study it was realized that the stability of certain factors in our institution would facilitate this analysis. Foremost was the fact that there was throughout the period in study a uniform concept of treatment—all cases of suspected acute appendicitis were operated upon and in each the offending organ was removed. Preoperative suspicion of perforation or evidence of abscess or peritonitis did not alter this concept. Operative therapy in the face

急性虫垂炎が疑われれば全例手術

急性虫垂炎に対する治療法の歴史



手術が95%を占める

JAMA Surg 2019; 154: 141-9.

急性虫垂炎に対する治療法の歴史

TREATMENT OF ACUTE APPENDICITIS

BY

ERIC COLDREY, M.D., F.R.C.S.
Consulting Surgeon, Rotherham Hospital

Br Med J. 1956 Dec 22;2(5007):1458-61.

from various parts of the world have written from time to time advocating conservative treatment in some of the more advanced cases.

Twenty-five years ago I began to treat cases of appendix abscess conservatively, and was surprised that most of them resolved without any operative help. Since the introduction of antibiotics I have continued this line of treatment and have usually found that it is not necessary to operate, for most cases settle down.

If with the help of antibiotics the human body could absorb an appendix abscess, I began to wonder whether it was capable of dealing with burst appendices that did not localize. Experiment soon showed that it could.

During the last four years I have asked that every case of acute appendicitis of over 24 hours' duration coming into hospital under me should be treated con-

1930年代から抗菌薬治療を導入

手術移行もほとんどなかった

過去のRCT（抗菌薬vs.手術）

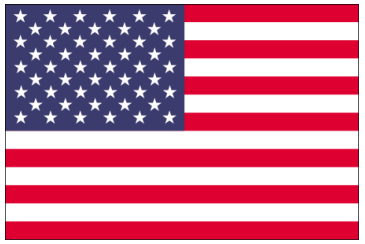
year	Journal	country	n	imaging	糞石症例	1年以内に 手術を要した割合
1995	Br J Surg	Sweden	40	US	不明	35%
2006	World J Surg	Sweden	252	なし	不明	24%
2009	Br J Surg	Sweden	369	US、CT （一部使用）	不明	48%
2011	Lancet	France	243	CT	include	37%
2015	JAMA	Finland	530	CT	exclude	27.3%

過去のRCT（抗菌薬vs.手術）

・多くの症例で抗菌薬治療により30日以内の手術移行は回避可能

・経験則により糞石は、穿孔や術後合併症のリスク因子とされ、
過去の大規模RCTでは除外されている

本日の論文①



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 12, 2020 VOL. 383 NO. 20

A Randomized Trial Comparing Antibiotics with Appendectomy for Appendicitis

The CODA Collaborative*

アメリカ25施設参加、前向き・非盲検化・ランダム化比較試験

手術に対する抗菌薬の非劣性試験

論文のPICO

P	Uncomplicated appendicitis
I	Antibiotics
C	Appendectomy
O	EQ-5D at 30-days

Statistical analysis

- ITT解析
- 虫垂切除術後のEQ-5D score：0.9±0.12と設定
- 非劣性マージン：-0.05、one-sided α：0.025

Criteria

-Inclusion criteria-

- 英語orスペイン語が話せる≥18歳
- 画像検査で急性虫垂炎と診断
- 糞石症例含む（subgroup化）
- 穿孔症例を含む

-Exclusion Criteria-

- Septic shock
- 汎発性腹膜炎
- 再発性虫垂炎
- 回結腸切除術が予見される高度炎症
- 膿瘍形成
- 腫瘍性病変が疑われる
- 免疫不全
- 非代償性肝硬変、炎症性腸疾患に対して服薬治療中
- 治療中の悪性腫瘍
- 感染性疾患に対して抗菌薬治療中
- 抗菌薬にアレルギーあり
- 1カ月以内に腹部/骨盤手術歴

treatment

抗菌薬治療群

・24時間の経静脈投与、その後経口投与計10日間
・抗菌薬指定なし（各ガイドラインを参照）

-手術移行基準-

・汎発性腹膜炎

・septic shock

・48時間以内の症状増悪

Figure S1. Most common antibiotics in the CODA trial

For initial intravenous use (at least 24 hours)

ertapenem
cefoxitin
or
metronidazole *plus one of the following*
- ceftriaxone
- cefazolin
- levofloxacin

For oral use (remainder of 10 total days)

metronidazole *plus one of the following*
- ciprofloxacin
- cefdinir

手術群

・開腹/腹腔鏡,手術手技の指定なし

・術前・術後治療は一般的管理

Primary outcome

European Quality of Life-5 Dimensions（EQ-5D）による30日目の健康状態

- 健康関連QOLの評価尺度として開発
- ”mobility” “self-care” “usual activities” “pain/discomfort” “anxiety/depression” の5項目に関して、1点（最良）～3点（最低）で評価

Guidelines for value sets in economic and on-economic studies using EQ-5D.
In The Measurement and Valuation of Health Status Using EQ-5D
: A European Perspective. the Netherlands Kluwer Academic Publishers; 2003:29–42.

Primary outcome

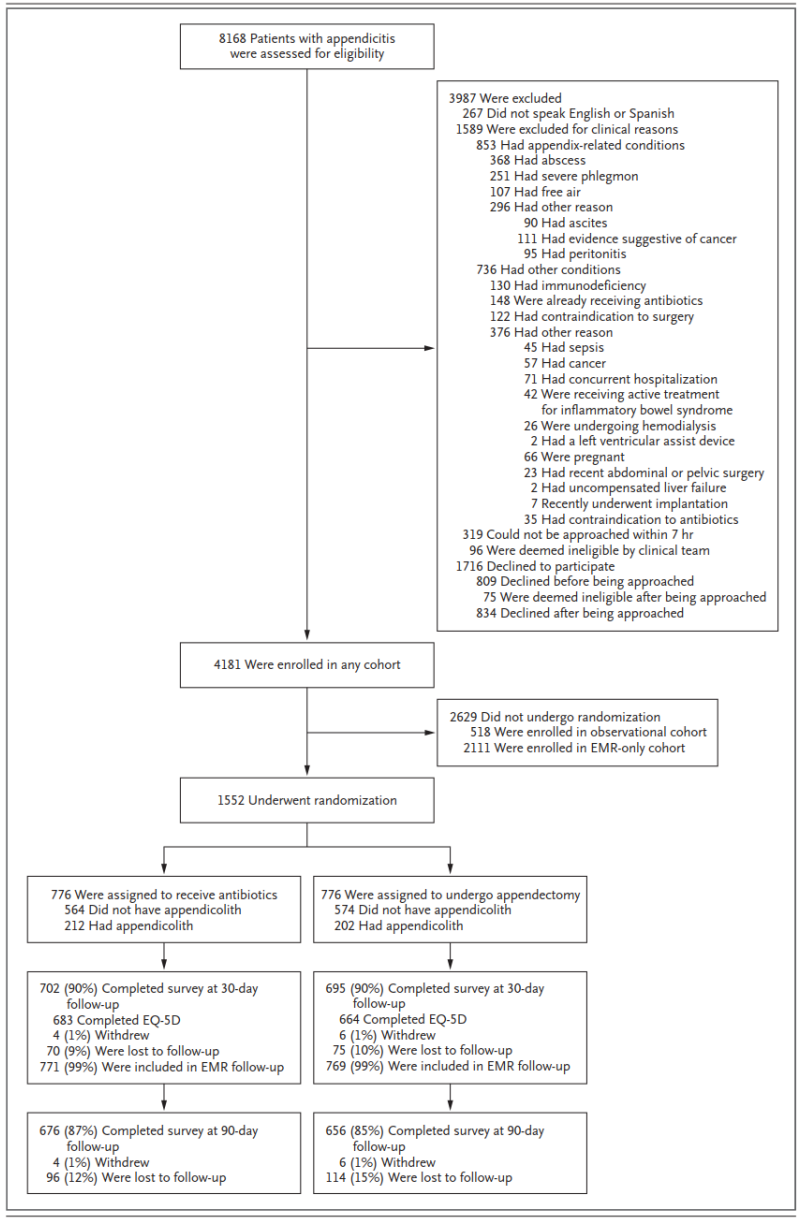
European Quality of Life-5 Dimensions（EQ-5D）による30日目の健康状態

状態	スコア	状態	スコア
11111	1. 000	12213	0. 638
11112	0. 786	12221	0. 670
11113	0. 736	12222	0. 608
11121	0. 768	12223	0. 558
11122	0. 705	12231	0. 494
11123	0. 656	12233	0. 444
11131	0. 654	12311	0. 661
11132	0. 592	12312	0. 599
11133	0. 542	12313	0. 549
:	:	:	:

- **換算表を用いてスコア算出**
- **最良1点（問題なく健康）**
  最低0点（死亡）

Tsuchiya A, Ikeda S, Ikegami N, et al. Estimating an EQ-5D population value set: the case of Japan. Health Econ. 2002;11(4):341-53.

Flow diagram



2016.5
-2020.2

8168, acute appendicitis

3987, excluded

1589, 臨床的因子

1716, Pt拒否

4181, enrolled

1552, randomization

776, antibiotics

776, surgery

背　景　因　子

Table 1. Sociodemographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Antibiotics (N=776)	Appendectomy (N=776)
Age — yr	38.3±13.4	37.8±13.7
Sex — no. (%)		
Female	286 (37)	290 (37)
Male	490 (63)	486 (63)
Gender different from sex assigned at birth — no. (%)	8 (1)	6 (1)
Race or ethnic group — no. (%)†		
White	461 (60)	449 (59)
Black	75 (10)	63 (8)
American Indian or Alaska Native	13 (2)	9 (1)
Asian	39 (5)	53 (7)
Native Hawaiian or Pacific Islander	4 (1)	3 (<1)
Multiple or other	176 (23)	185 (24)
Hispanic ethnic group†	362 (47)	366 (47)
Primary language — no. (%)		
English	469 (60)	464 (60)
Spanish	267 (34)	267 (34)
Other	40 (5)	45 (6)
Insurance — no. (%)		
Commercial	323 (43)	317 (42)
Medicare or Tricare	89 (12)	89 (12)
Medicaid or other state program	134 (18)	131 (17)
Other or no coverage	213 (28)	217 (29)
Modified Charlson comorbidity index score‡	0.24±0.53	0.24±0.53
Body-mass index§	29.0±6.6	28.6±6.1
Duration of symptoms — days	1.8±3.6	1.6±1.6
Alvarado score¶	6.6±1.6	6.7±1.7
History of fever — no. (%)	194 (25)	185 (24)
Initial white-cell count — per μl	12,900±4000	13,400±4100
Imaging test — no. (%)		
Computed tomography alone	626 (81)	609 (78)
Ultrasonography alone	24 (3)	30 (4)
>1 Imaging test	125 (16)	137 (18)

	Antibiotics	Appendectomy
年齢	38.3±13.4	37.8±13.7
BMI	29.0±6.6	28.6±6.1
CT	97%	96%

結　果　-primary　outcome-

Table 2. Intention-to-Treat Comparison of Patient-Reported Outcomes, Clinical Outcomes, Time Spent in Health Care Settings, and Missed Work.*

Outcome	Overall			Appendicolith Present			Appendicolith Absent		
	Antibiotics	Surgery	Effect (95% CI)	Antibiotics	Surgery	Effect (95% CI)	Antibiotics	Surgery	Effect (95% CI)
EQ-5D at 30 days†‡	0.92±0.13	0.91±0.13	0.01 (−0.001 to 0.03)§	0.92±0.14	0.92±0.13	−0.01 (−0.03 to 0.02)§	0.92±0.13	0.91±0.13	0.02 (0.003 to 0.03)§

30日目のEQ-５D scoreに有意差なし

Subgroup解析（糞石の有無）でも同様の結果

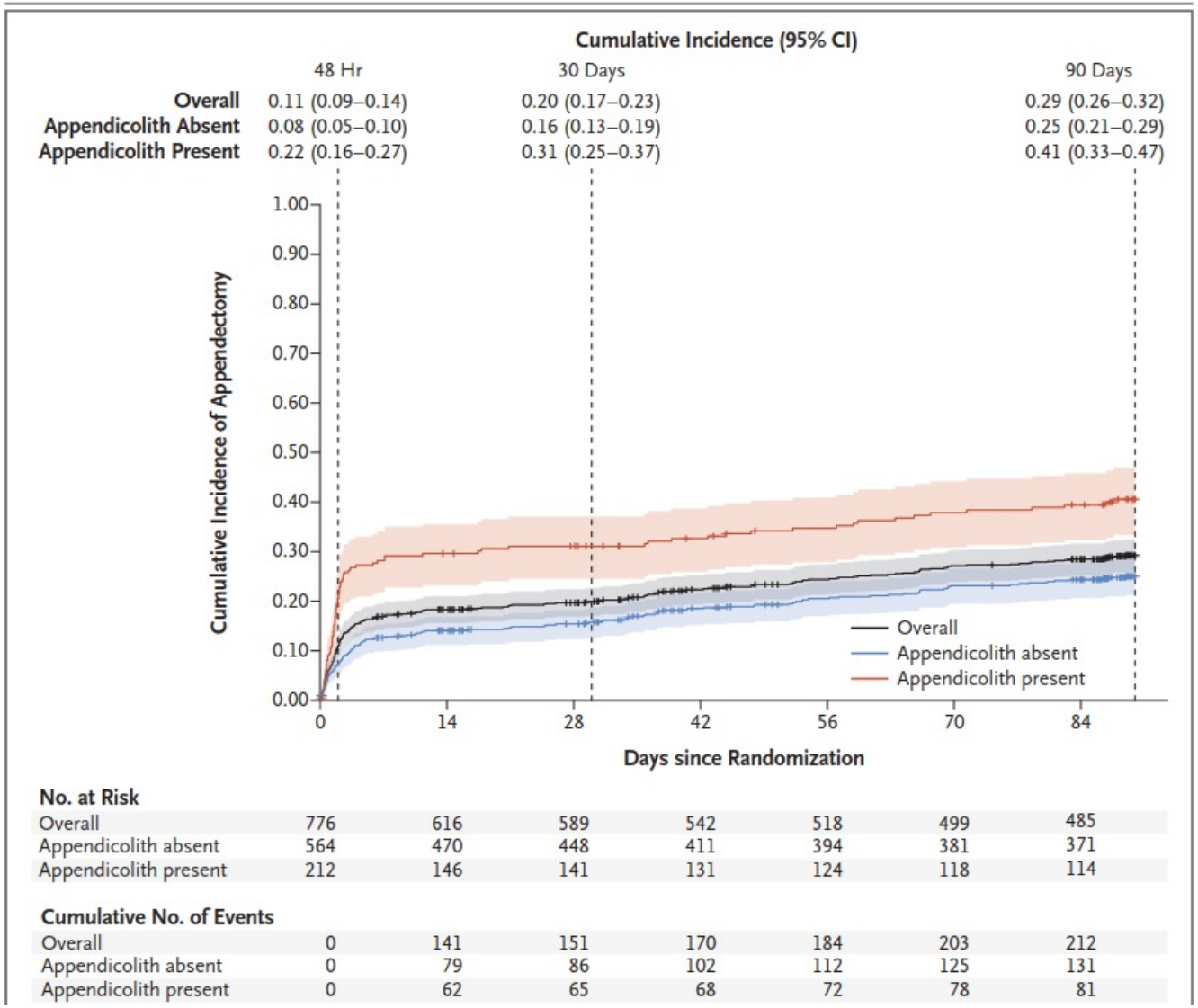
結　果　-secondary　outcome-

Outcome	Overall			Appendicolith Present			Appendicolith Absent		
	Antibiotics	Surgery	Effect (95% CI)	Antibiotics	Surgery	Effect (95% CI)	Antibiotics	Surgery	Effect (95% CI)
Days from randomization to discharge for index treatment — no. of days/ no. of participants (mean)‡	1030/776 (1.33)	1010/776 (1.30)	1.00 (0.89 to 1.13)††	403/212 (1.90)	330/202 (1.63)	1.15 (0.89 to 1.47)††	626/564 (1.11)	679/574 (1.18)	0.92 (0.82 to 1.05)††
Any hospitalization after index treatment within 90 days — no./total no. (%)‖	154/635 (24)	32/613 (5)	4.62 (3.21 to 6.65)**	57/176 (32)	8/157 (5)	6.36 (3.13 to 12.90)**	97/459 (21)	24/456 (5)	4.02 (2.62 to 6.16)**
Days in hospital after index treatment within 90 days — no. of days/ no. of participants (mean)‡	421/622 (0.68)	93/609 (0.15)	4.38 (2.49 to 7.73)††	191/166 (1.15)	37/156 (0.24)	4.55 (1.46 to 14.18)††	230/456 (0.50)	56/453 (0.12)	4.07 (2.24 to 7.41)††
Any visit to emergency department or urgent care clinic after index treatment within 90 days — no./ total no. (%)‖	55/618 (9)	26/604 (4)	2.07 (1.32 to 3.25)**	14/165 (8)	2/153 (1)	6.49 (1.50 to 28.09)**	41/453 (9)	24/451 (5)	1.70 (1.05 to 2.77)**
Visits to emergency department or urgent care clinic after index treatment within 90 days — no. of visits/ no. of participants (mean)‡	66/615 (0.11)	24/599 (0.04)	2.64 (1.57 to 4.43)††	17/163 (0.10)	2/153 (0.01)	8.19 (2.03 to 33.00)††	49/452 (0.11)	22/446 (0.05)	2.15 (1.23 to 3.76)††
Days of missed work for participant within 90 days — no. of days/ no. of participants (mean)‡	2516/478 (5.26)	4131/473 (8.73)	0.63 (0.51 to 0.77)††	743/121 (6.14)	1134/125 (9.07)	0.72 (0.48 to 1.09)††	1773/357 (4.97)	2997/348 (8.61)	0.60 (0.48 to 0.76)††
Days of missed work for caregiver within 90 days — no. of days/no. of care-givers (mean)‡	679/509 (1.33)	1009/495 (2.04)	0.66 (0.48 to 0.91)††	242/137 (1.77)	213/126 (1.69)	1.04 (0.56 to 1.92)††	437/372 (1.17)	796/369 (2.16)	0.56 (0.38 to 0.82)††

入院期間、欠勤日数、介護者の欠勤日数に有意差なし

治療開始後の救急受診割合は抗菌薬群の方が高い

抗菌薬治療群の累積手術移行率



	48時間	30日	90日
全体	11%	20%	29%
糞石（−）	8%	16%	25%
糞石（+）	22%	31%	41%

結　論

糞石を含むUncomplicated appendicitisに対する**抗菌薬治療**は**手術療法と比較して非劣性**であった

抗菌薬治療は、70%以上が手術を回避でき、本人・介護者の欠勤日数も短くなる長所があることから、手術療法の代用になり得る

AMERICAN COLLEGE OF SURGEONS
Inspiring Quality:
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COVID 19: Elective Case Triage Guidelines for Surgical Care

Emergency General Surgery

Revised 12/8/2020

Appendicitis, Uncomplicated

There is high-quality evidence that most patients with appendicitis can be managed with antibiotics instead of appendectomy (69 percent overall avoid appendectomy by 90 days, 75 percent of those without appendicolith, and 59 percent of those with appendicolith). Based on the surgeon's judgment, patient preferences, and local resources (e.g., hospital staff, bed, and PPE supply availability) antibiotics are an acceptable first-line treatment, with appendectomy offered for those with worsening or recurrent symptoms. Length of time in the hospital setting was similar between treatments, but nearly half of patients receiving antibiotics were not admitted to the hospital. Antibiotics resulted in more 90-day emergency room visits and hospitalizations. Antibiotics were associated with a higher risk of complications in those with an appendicolith.

本日の論文②

Research

JAMA Surgery | Original Investigation

Patient Factors Associated With Appendectomy Within 30 Days of Initiating Antibiotic Treatment for Appendicitis

Writing Group for the CODA Collaborative

CODA trialデータを用いた

30日以内に抗菌薬治療から手術移行するリスク因子の検証

研究手法

・CODA trial登録症例のうち30日時点の状況を調査

・手術移行症例と非移行症例について背景因子、血液検査結果、画像所見を比較

・4つの多変量解析モデルを作成

-base model- 年齢、性別、BMI、病悩期間、pain score、WBC、発熱、
嘔気・嘔吐・食思不振

-base + A ＝base model＋糞石

-base + R ＝base model+虫垂径、穿孔、膿瘍、脂肪織濃度上昇

-base +R+A＝base model + 糞石、虫垂径、穿孔、膿瘍、脂肪織濃度上昇

これらをWald testで比較し、あてはまりが良いもので多変量解析

Characteristics①

Table 1. Demographic and Clinical Characteristics of Participants Randomized to Antibiotics by Appendectomy Status at 30 Days

Characteristic	No. (%)[a]		
	Overall (n = 776)	Underwent appendectomy within 30 d: Yes (n = 154)	Underwent appendectomy within 30 d: No (n = 581)
Age, y			
Mean (SD)	38.3 (13.4)	38.8 (13.7)	38.0 (13.2)
≥50	150 (19)	32 (21)	104 (18)
<50	626 (81)	122 (79)	477 (82)
Sex			
Female	286 (37)	61 (40)	211 (36)
Male	490 (63)	93 (60)	370 (64)
Race			
American Indian or Alaska Native	13 (2)	4 (3)	6 (1)
Asian	39 (5)	10 (6)	29 (5)
Black	75 (10)	16 (11)	58 (10)
Native Hawaiian or Pacific Islander	4 (1)	1 (1)	2 (<1)
White	461 (60)	79 (52)	359 (63)
Multiple or other[b]	176 (23)	43 (28)	120 (21)
Hispanic			
No	414 (53)	77 (50)	321 (55)
Yes	362 (47)	77 (50)	260 (45)

776例のうち、検証可能なデータは735例

154例（21%）が30日以内に手術移行

平均年齢は38歳、50歳未満が80%前後

男性の割合が高い

Characteristics②

Health literacy help			
Never or rarely	608 (81)	115 (76)	466 (83)
Sometimes or more	141 (19)	36 (24)	93 (17)
Worried about bills			
No	217 (29)	37 (24)	168 (30)
Yes	545 (72)	116 (76)	402 (71)
Below federal poverty level or Medicaid beneficiary			
No	315 (54)	54 (47)	251 (57)
Yes	273 (46)	61 (53)	190 (43)
Modified Charlson comorbidity score, mean (SD)	0.2 (0.5)	0.3 (0.7)	0.2 (0.5)
BMI			
<25	178 (30)	35 (25)	138 (32)
25-<30	198 (33)	51 (36)	132 (31)
30-<35	128 (21)	35 (25)	85 (20)
≥35	98 (16)	19 (14)	77 (18)
Alvarado score, mean (SD)	6.6 (1.6)	7.0 (1.5)	6.5 (1.6)
Duration of symptoms, d			
<1	195 (25)	39 (26)	145 (25)
≥1	580 (75)	114 (75)	436 (75)
Pain in previous 7 d, mean (SD)	5.4 (3.0)	5.9 (3.2)	5.3 (2.9)
White blood cell count, mean (SD), /μL	12 900 (4000)	13 500 (3900)	12 800 (4000)
Fever			
None or NR	582 (75)	108 (70)	443 (76)
Reported	194 (25)	46 (30)	138 (24)

(continued)

	手術移行あり	手術移行なし
BMI≧25	75%	68%
病悩期間≧1日	75%	75%
WBC	13500	12800
発熱あり	30%	24%

Characteristics③

Table 1. Demographic and Clinical Characteristics of Participants Randomized to Antibiotics by Appendectomy Status at 30 Days (continued)

Characteristic	No. (%)[a]		
	Overall (n = 776)	Underwent appendectomy within 30 d: Yes (n = 154)	Underwent appendectomy within 30 d: No (n = 581)
Nausea, vomiting, or anorexia			
None or NR	134 (17)	32 (21)	97 (17)
Reported	641 (83)	122 (79)	483 (83)
Imaging test			
Computed tomography alone	626 (81)	124 (81)	468 (81)
Ultrasonography alone	24 (3)	6 (4)	18 (3)
>1 imaging test	125 (16)	23 (15)	95 (16)
Magnetic resonance imaging	1 (<1)	1 (1)	0 (0)
Appendicolith			
None or NR	564 (73)	89 (58)	443 (76)
Reported	212 (27)	65 (42)	138 (24)
Appendiceal diameter, mean (SD), mm	11.5 (2.9)	12.3 (3.1)	11.3 (2.8)
Perforation, abscess, or appendiceal fat stranding present			
None or NR	646 (86)	123 (84)	487 (87)
Reported	102 (14)	24 (16)	73 (13)

	手術移行あり	手術移行なし
CT scan	96%	97%
糞石	42%	24%
虫垂径	12.3mm	11.3mm
穿孔/膿瘍/脂肪織濃度上昇	16%	13%

手術移行の原因

Table 2. Primary Reason for Appendectomy Among Participants Who Had an Appendectomy Within 30 Days

Reason	No (%) (n = 150)[a]
Acute clinical	116 (77)
Worsening of symptoms	88 (59)
Continuing symptoms	
≤48 h	18 (12)
>48 h	10 (7)
Nonacute clinical	2 (1)
Nonclinical	32 (21)
Worry or concern for recurrence	10 (7)
Planned interval appendectomy	3 (2)
Consultation with friend or family	9 (6)
Other[b]	10 (7)

- 急性期臨床的要因　77%（116）
  - 症状増悪　59%（88）
  - 症状持続 ≤48hr　12%（12）
  - >48hr　7%（7）
- 非急性期臨床的要因　1%（2）
- 非臨床的要因　21%（32）
  - 再発の心配　7%（10）
  - 予定手術　2%（3）
  - 家族友人と相談　6%（9）
  - その他　7%（10）

単変量&多変量解析

Table 3. Factors Associated With 30-Day Appendectomy in Univariate and Multivariable Models

Factor	Odds ratio (95% CI)[a]	
	Univariate	Base + R + A
Age, per 1-y increase	1.01 (0.99-1.02)	1.00 (0.98-1.01)
Female sex (vs male sex)	1.16 (0.80-1.68)	1.53 (1.01-2.31)
BMI (vs <25)		
25-35	1.77 (1.14-2.75)	1.60 (0.99-2.60)
>35	0.75 (0.42-1.34)	0.68 (0.37-1.24)
Symptoms duration ≥1 d (vs <1 d)	0.89 (0.58-1.36)	0.81 (0.51-1.31)
Mean pain in the previous 7 d, per 1-point increase	1.07 (1.00-1.14)	1.06 (0.99-1.14)
White blood cell count, per 1000-cells/μL increase	1.04 (0.99-1.09)	1.03 (0.98-1.09)
Fever[b]	1.31 (0.87-1.97)	1.28 (0.82-1.98)
Nausea, vomiting, or anorexia[b]	0.83 (0.52-1.32)	0.69 (0.42-1.16)
Appendiceal diameter, per 1-mm increase	1.14 (1.06-1.22)	1.09 (1.00-1.18)
Perforation, abscess, or fat stranding[b]	1.56 (0.94-2.59)	1.14 (0.66-1.98)
Appendicolith[b]	2.56 (1.73-3.79)	1.99 (1.28-3.10)

30日以内に手術移行となる有意なリスク因子

糞石　Odds **1.99** (1.28-3.10)

虫垂径　Odds **1.09** (1.00-1.18)

女性　odds **1.53** (1.01-2.31)

Discussion

- **糞石（＋）で約2倍の手術移行リスク**

  ⇒抗菌薬治療を考慮する際、糞石の有無を画像で検索することが重要

  USよりCTの方が検出力に優れるが、世界的にはＵＳの使用率が依然高い

  ＣＴによる糞石検出の感度は低い[1)]（55%）＋放射線被爆が問題

1) Curr Probl Diagn Radiol. 2018;47(1):6-9.

- **女性がリスク因子**となった

  初診時の誤診、鎮痛薬不足[2)]、出産に対する影響を懸念

  ⇒negative appendectomyの増加が影響している可能性がある

  ⇒治療法判断に用いるべき因子ではない

2) Acad Emerg Med. 2008;15(5):414-418.

Limitation

・手術移行した理由が単一ではない

→身体症状のみ and/or 担当医の意向が反映か、見分けがつかない

・初発虫垂炎の経過に焦点⇒観察期間を30日

しかし、この期間で再発した症例を含んでいる可能性がある

・低頻度であった膿瘍形成・穿孔・脂肪濃度上昇を1つの変数にまとめた

Conclusion

糞石は、抗菌薬治療開始後、**30日以内に手術移行**となる

予測因子であり、急性虫垂炎の治療方針決定に有用な情報である

Antibiotics *versus* placebo in adults with CT-confirmed uncomplicated acute appendicitis (APPAC III): randomized double-blind superiority trial

Paulina Salminen[1,2,*], Suvi Sippola[1,2,3], Jussi Haijanen[1,2], Pia Nordström[4,5], Tuomo Rantanen[6,7], Tero Rautio[8,9], Ville Sallinen[10], Eliisa Löyttyniemi[11], Saija Hurme[11], Ville Tammilehto[12], Johanna Laukkarinen[4,5], Heini Savolainen[6,7], Sanna Meriläinen[8,9], Ari Leppäniemi[10] and Juha Grönroos[1,2]

Br J Surg.2022.109.503-509

-Uncomplicated appendicitis（糞石(＋)は除く）に対する

抗菌薬治療の有用性を検証する優越性試験

-多施設、二重盲検、ランダム化比較試験

Antibiotics *versus* placebo in adults with CT-confirmed uncomplicated acute appendicitis (APPAC III): randomized double-blind superiority trial

Paulina Salminen[1,2,*], Suvi Sippola[1,2,3], Jussi Haijanen[1,2], Pia Nordström[4,5], Tuomo Rantanen[6,7], Tero Rautio[8,9], Ville Sallinen[10], Eliisa Löyttyniemi[11], Saija Hurme[11], Ville Tammilehto[12], Johanna Laukkarinen[4,5], Heini Savolainen[6,7], Sanna Meriläinen[8,9], Ari Leppäniemi[10] and Juha Grönroos[1,2]

Br J Surg.2022.109.503-509

Primary outcome ：10日目における治療奏功割合

Antibiotics(n=35) vs. placebo (n=31)

＝97% (92-100) vs. 87% (75-99)

difference 10% （0.9-21, p=0.14）

結　論

抗菌薬治療の優越性を示せなかった⇒placeboの非劣性試験が必要

RESEARCH Open Access

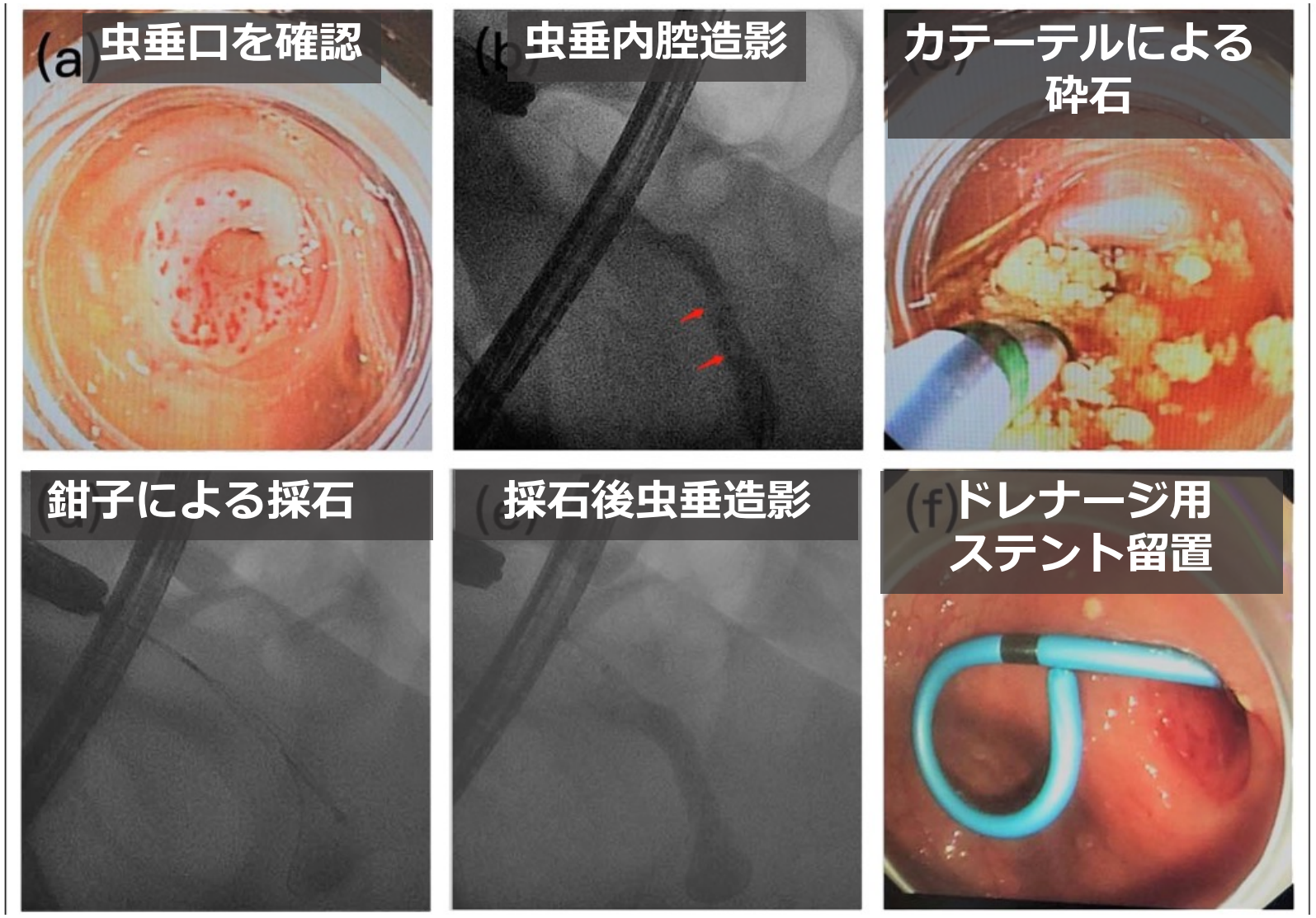
Endoscopic retrograde appendicitis therapy versus laparoscopic appendectomy versus open appendectomy for acute appendicitis: a pilot study

Zhemin Shen[1], Peilong Sun[1*†], Miao Jiang[2†], Zili Zhen[1], Jingtian Liu[1], Mu Ye[1] and Weida Huang[1]

Shen *et al. BMC Gastroenterology* (2022) 22:63
https://doi.org/10.1186/s12876-022-02139-7

内視鏡治療と腹腔鏡手術と開腹手術を比較

急性虫垂炎に対する内視鏡治療（ERAT）



総胆管結石に対する

ERBD手技の応用

2012年Liuらが考案

Gastrointest Endosc.2012.76.862-6

Results

Table 2 Clinical outcome

	ERAT group (n = 33)	LA group (n = 33)	OA group (n = 33)	*P* value
Treatment Success, n (%)	29 (87.88)	32 (96.97)	33 (100)	0.123

ERATの成功率は88%（29/33）

4例は虫垂へのカニュレーション困難にて手術移行

3群間で治療成功率に有意差なし

Results

Table 3 Follow-up

	ERAT group (n = 33)
Stent discharged, n (%)	29 (87.88)
Spontaneously discharged, n (%)	9 (31.03)
Retrieved, n (%)	20 (68.97)
Adverse events, n (%)	3 (9.09)
Recurrence, n (%)	3 (9.09)
Patients with appendicolith at first admission, n (%)	2 (6.06)
Patients without appendicolith at first admission, n (%)	1 (3.03)
Crossover rate (%)	21.21
Complications	
Wound infection, n (%)	NA
Abdominal or incisional pain, n (%)	NA
Abdominal fluid collection, n (%)	NA
Obstructive symptoms, n (%)	NA

全例ステント抜去
内視鏡的抜去　69%
自然抜去　　31%

ERAT完遂29例のうち
3例（10%）が再発
（4,6,11カ月目）

初回治療時に糞石あり2例
糞石なし1例

RESEARCH Open Access

Endoscopic retrograde appendicitis therapy versus laparoscopic appendectomy versus open appendectomy for acute appendicitis: a pilot study

Zhemin Shen[1], Peilong Sun[1*†], Miao Jiang[2†], Zili Zhen[1], Jingtian Liu[1], Mu Ye[1] and Weida Huang[1]

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結　論

- ERATは有用な治療法の一つである
- 虫垂内腔へのカニュレーション操作の難易度の高さと術後再発率が課題
- 大規模RCTが望まれる

TAKE HOME MESSAGE

・単純性虫垂炎に対する**抗菌薬治療**により、**80%**が**手術回避**。

しかし、**糞石**を認める症例は、**手術移行リスク**が**約2倍**となる。

・軽症症例に対する抗菌薬の優越性は示されていない。

・保存的療法の選択肢として、内視鏡的治療（ERAT）が普及するかもしれない

British Journal of Surgery 1995, **82**, 166–169

Randomized controlled trial of appendicectomy *versus* antibiotic therapy for acute appendicitis

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Correspondence to: Dr S. Eriksson

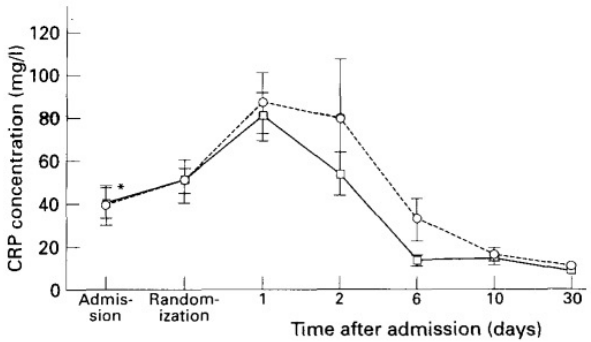
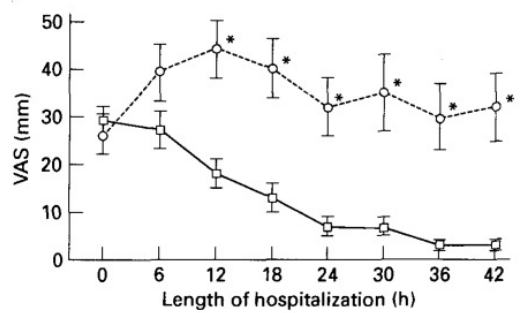


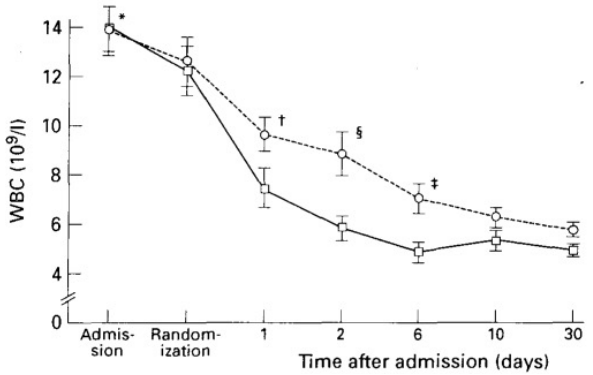
Fig. 1 Mean(s.e.m.) concentration of C-reactive protein (CRP) in patients with acute appendicitis treated with antibiotics (□) or surgery (○) during hospitalization and at 30 days of follow-up. *$P < 0{\cdot}001$ (admission *versus* randomization, Student's t test)



No. of patients

Antibiotics	20	20	18	19	19	19	18	18
Surgery	20	16	16	20	13	12	11	10

Fig. 3 Pain recorded using a visual analogue scale (VAS) by patients



抗菌薬治療群（N=20）　　手術療法群（N=20）

2日以内に19人退院
1日は穿孔のため入院中に手術

7人は退院後に虫垂炎再燃

Exclusion
・septic shock
・汎発性腹膜炎
・再発症例
・画像上、重症炎症合併
・膿瘍形成
・free air(+)
・腫瘍疑い

Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial

Corinne Vons, Caroline Barry*, Sophie Maitre*, Karine Pautrat, Mahaut Leconte, Bruno Costaglioli, Mehdi Karoui, Arnaud Alves, Bertrand Dousset, Patrice Valleur, Bruno Falissard, Dominique Franco

Lancet 2011; 377: 1573–79

See Comment page 1545

Uncomplicated appendicitis （虫垂径6mm以上）
除外：壁外ガス、傍虫垂液体貯留、広範囲腹水、虫垂径15mm以上

手術群
・麻酔導入時にamoxicillin + clavulanic acid 2g
・開腹or腹腔鏡
・術後抗菌薬なし

抗菌薬群
・amoxicillin + clavulanic acid 3g（IV or OI）
・48hrで改善なければ手術移行
・症状改善次第、退院
・退院後も8日目まで同様の抗菌薬継続
・Day8, 15, 30, 90, 180, 360にフォロー

Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial

Corinne Vons, Caroline Barry*, Sophie Maitre*, Karine Pautrat, Mahaut Leconte, Bruno Costaglioli, Mehdi Karoui, Arnaud Alves, Bertrand Dousset, Patrice Valleur, Bruno Falissard, Dominique Franco

Lancet 2011; 377: 1573–79

See Comment page 1545

Primary endpoint
治療開始30日以内の腹膜炎発症率

Secondary endpoint
VAS score≥4の日数
在院日数
欠勤日数
1年以内の合併症（創感染、瘢痕ヘルニア、腸閉塞）
虫垂炎再発（day30~1y）

Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial

Corinne Vons, Caroline Barry, Sophie Maitre*, Karine Pautrat, Mahaut Leconte, Bruno Costaglioli, Mehdi Karoui, Arnaud Alves, Bertrand Dousset, Patrice Valleur, Bruno Falissard, Dominique Franco*

Lancet 2011; 377: 1573–79

See Comment page 1545

Summary

	Appendicectomy group (n=119)	Antibiotic-treatment group (n=120)	Difference (95% CI)
Primary endpoint events			
30-day post-therapeutic peritonitis	2 (2%)*	9 (8%)†	5·8 (0·3 to 12·1)
Incidence of peritonitis			
Complicated appendicitis with peritonitis identified at surgery	21 (18%)‡	9 (8%)†	−10·1 (−18·7 to −1·7)
Postoperative peritonitis	2 (2%)‡	2 (2%)§	0 (−4·4 to 4·4)

Data are number unless otherwise stated. *In the appendicectomy group, two cases of postoperative peritonitis occurred; these patients had postoperative localised peritonitis successfully treated with antibiotics. †In the antibiotic group, complicated appendicitis with peritonitis was identified during appendicectomy performed within 30 days of treatment initiation in nine of 14 patients who did not show improvement. ‡Discovery of a complicated appendicitis with peritonitis in the appendicectomy group was not a primary endpoint. §Two patients in the antibiotic group, who underwent secondary appendicectomy, had postoperative peritonitis.

***Table 2*: Incidence of primary endpoint events and complicated appendicitis with peritonitis and postoperative peritonitis within 30 days after the start of treatment in both groups (intention-to-treat population)**

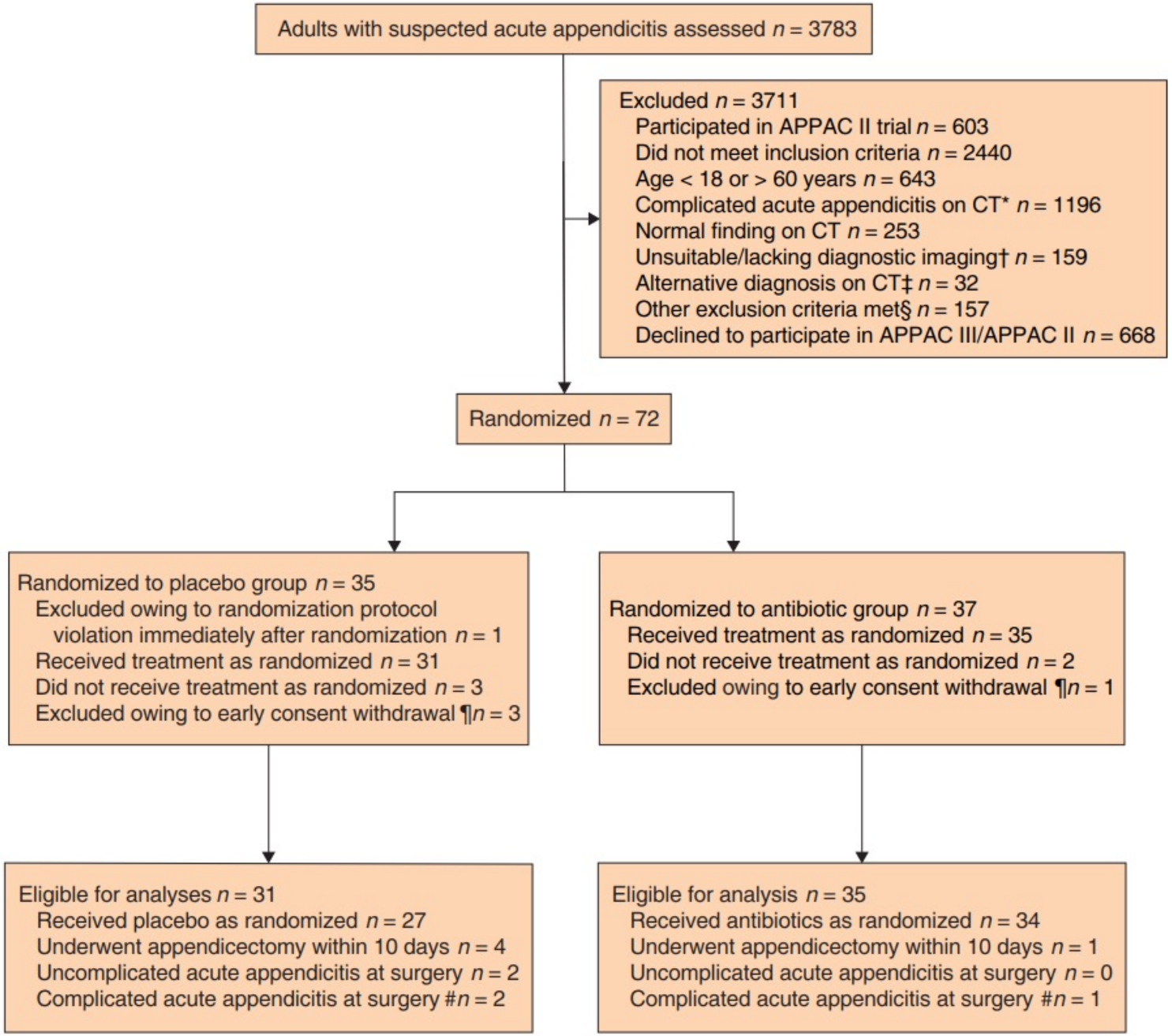


Fig. 1 Flow chart for APPAC III trial

18-60歳
CTでuncomplicated appendicitis
ー虫垂径≥6mm
ー壁肥厚あり
ー虫垂周囲の浮腫を伴う
ー糞石がない
ー穿孔がなし
ー膿瘍なし
ー腫瘍性病変の疑いなし

抗菌薬群

Ertapenem 1g/day×3days
＋
Levofloxacin 500mg/day
Metronidazole 500mg×3/day　×4days

Placebo群

抗菌薬群と同様のタイミングで投与

安全を期して入院期間は最低3日間

治療効果なし⇒腹腔鏡手術

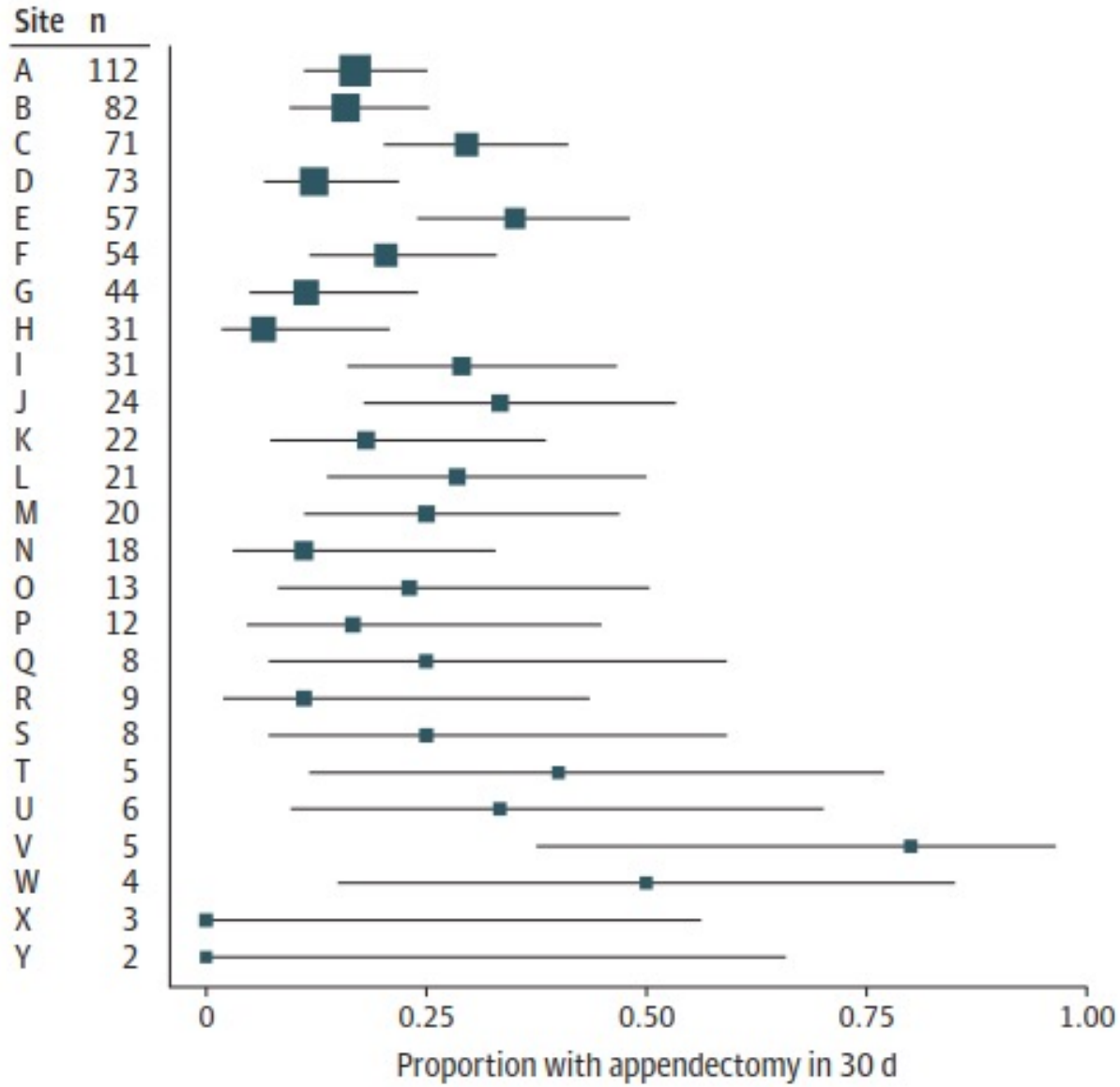
10日目での治療奏効率

抗菌薬vs. placebo= 97%（92-100%) vs. 87%（75-99%)

奏効率の差：10%（90% C.I 0.9-21、p=0.14）

抗菌薬治療の優性なし
→抗菌薬に対するplaceboの非劣性試験を行うべき

Figure. Unadjusted Proportion of Participants With Appendectomy Within 30 Days by Practice Site

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尾田栄一郎 原作
横内謙介 脚本演出
市川猿之助 演出
市川猿翁 スーパーバイザー
2017年
10月6日（金）～11月25日（土）
新橋演舞場
製作 松竹
日本全国で20万人を動員した大ヒット歌舞伎がさらなる進化を遂げて新橋演舞場に帰ってくる!!
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市川弘太郎
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