ORIGINAL ARTICLE

If not appendicitis, then what else can it be? A retrospective review of 1492 appendectomies

CME

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Objective To audit the appendectomies at our institute, and summarise atypical pathological results with a discussion of appropriate management.

Design Retrospective study.

Setting Regional hospital, Hong Kong.

Patients All patients who underwent appendectomy for presumed acute appendicitis from June 2003 to June 2008 were recruited. Incidental appendectomy was excluded. Patient demographics, pathological findings, and surgical outcomes were analysed.

Results The overall negative appendectomy rate was 18.2%. Female patients of reproductive age (11-50 years) conferred an independent risk for a higher negative appendectomy rate than other females (28.7% vs 11.5%; P<0.001). The overall perforation rate was 22.5%; the extremes of age (<11 or >70 years) conferred an independent risk of perforated appendicitis (25.2% vs 16.3%; P=0.002). Preoperative imaging was not associated with a lower negative appendectomy rate or rate for perforated appendicitis (P=0.205 and 0.218, respectively). Multivariate analysis suggested that a preoperative white cell count of less than 13.5 x 10^9/L was an independent predictor of negative appendectomy (P<0.001); the body temperature and pulse rate of the patients with perforated appendicitis were higher than in those without perforation (P=0.004 and 0.003, respectively). Only 4.0% of the appendectomy specimens contained other appendiceal pathologies. Appendiceal diverticulitis was the most common inflammatory pathology, contributing to 2.7% of all appendectomies, followed by granulomatous appendicitis. In this series there were eight carcinoid tumours, three adenocarcinomas, two mucinous cystadenomas; tubular adenoma, metastatic deposition, mucinous cystadenocarcinoma and pseudomyxoma peritonei each occurred in one patient only.

Conclusions A more focused utilisation of preoperative imaging in females of reproductive age and patients at the extremes of age is suggested. Long-term follow-up should be offered to patients with granulomatous appendicitis and neoplastic appendiceal diseases.

Key words
Appendectomy; Appendicitis; Diagnostic errors; Diagnostic imaging; Granuloma

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Introduction

The life-time risk of acute appendicitis is around 7%, which makes appendectomy one of the most commonly performed operations. Since typical presentations are only encountered in about 60% of patients, accurate preoperative diagnosis has long been a great challenge, even to experienced surgeons. Various imaging modalities, biochemical markers, and scoring systems have been introduced, with a view to lower the negative appendectomy rate (NAR). However, there is continuing controversy about their routine use. While studies are still ongoing to investigate how to improve the diagnostic accuracy, certain unexpected/unusual lesions of the appendix may warrant further clinical attention or follow-up. This study reviewed appendectomies for presumed acute appendicitis over a 5-year period, and entailed auditing of all such surgeries performed in our hospital. By this means we set out to determine the incidence and relationships of various pathological

findings to different demographic characteristics. A literature review covering the management of these conditions was also performed.

Methods

Patients in this study were recruited from Queen Elizabeth Hospital which is a regional hospital as well as a tertiary surgical referral centre. The records of all those who underwent either laparoscopic or open appendectomy from 30 June 2003 to 30 June 2008 for presumed acute appendicitis were retrieved from the hospital database. All those who had appendectomy performed on a non-emergency basis or as a part of other surgical procedures (eg right hemicolectomy for carcinoma of the caecum and incidental appendectomy) were excluded. The records of 1492 patients were retrieved in this retrospective study and all the medical notes, operative records, and pathology reports were reviewed. The diagnosis of acute appendicitis was confirmed if there was infiltration with polymorphs in the muscularis propria of the appendix. Perforation was defined either intra-operatively by the surgeon, or described in the pathology report. Periappendicitis, fibrous obliteration, and serositis were regarded as negative appendectomies. We defined the reproductive age-group as females aged 11 to 50 years, and the extremes of age as being less than 11 or greater than 70 years. Statistical analysis was performed using the Statistical Package for the Social Sciences (Windows version 10.0; SPSS Inc, Chicago [IL], US). Categorical variables were compared using the Chi squared test while continuous variables were compared using *t* tests. Results with P value of less than 0.05 were considered statistically significant.

假如不是闌尾炎，會是什麼病症？1492宗闌尾切除術的病例回顧

目的 審視本院的闌尾切除術病例，概述非典型病理學檢驗結果，並討論醫治該症的適當方法。

設計 回顧研究。

安排 香港一所地區醫院。

患者 研究的病例為2003年6月至2008年6月因推定患上急性闌尾炎而接受闌尾切除術的患者，但不包括附帶性闌尾切除術的個案。分析項目包括患者的人口統計數據、病理學檢驗結果、手術結果。

結果 闌尾炎誤診手術總體比率為18.2%。與其他年齡的女性患者比較，處於生育年齡（即11-50歲）是闌尾炎誤診手術比率較高的獨立風險因子（11.5%比28.7%；P<0.001）。穿孔總比率為22.5%，而年齡小於11歲或大於70歲則為穿孔性闌尾炎的獨立風險因子（25.2%比16.3%；P=0.002）。術前造影並不能減低闌尾炎誤診手術或穿孔性闌尾炎的比率（P依次為0.205及0.218）。多變量分析結果顯示，術前白血球數量少於13.5 x 10^9/L為闌尾炎誤診手術的獨立預測因子（P<0.001）；穿孔性闌尾炎患者的體溫及脈搏均高於無穿孔的患者（P依次為0.004及0.003）。闌尾切除術取得的抽樣樣本中，僅有4%含其他與闌尾有關的異常情況。闌尾憩室炎是最常見的炎症病理徵狀，約佔闌尾切除術病例的2.7%，肉芽腫性闌尾炎則佔第二位。本研究中，有類癌8例、腺癌3例、黏液性囊腺癌2例，以及管狀腺瘤、轉移性沉積、黏液性囊腫腺癌、腹膜假黏液瘤各1例。

結論 本研究建議，應特別針對處於生育年齡的女性，以及年齡小於11歲或大於70歲的病者進行術前造影。此外，醫院亦應對肉芽腫性闌尾炎和腫瘤性闌尾疾病的患者作長期隨訪。

Results

During the 5-year period, there were 1492 emergency appendectomies. The number performed each year remained similar and the average number performed annually was 298 (Figs 1 and 2). There were 1162 patients with pathologically confirmed acute appendicitis; 601 were male and 561 were female, giving a sex ratio of 1.1 to 1. The median age of the patients with acute appendicitis was 38 (male 38.8, female 40.8; range, 3-96) years. The number of laparoscopic appendectomies performed was increasing, from 35% in 2003-04 to 73% in 2007-08. The median length of hospital stay was 4 (range, 1-91) days. Patients who had laparoscopic surgery had shorter mean stays than those who received open surgery (4.5 days vs 5.7 days; P<0.001). In all, 271 appendices were normal, making the overall NAR 18.2%; 13.0% in males and 23.1% in females (P<0.001). Notably, female patients of reproductive age (11-50 years) had a higher NAR than those in the non-reproductive age-group (28.7% vs 11.5%; P<0.001). After excluding reproductive-age females, the NAR was similar in both sexes (P=0.583). In the 1162 patients with confirmed acute appendicitis, the overall perforation

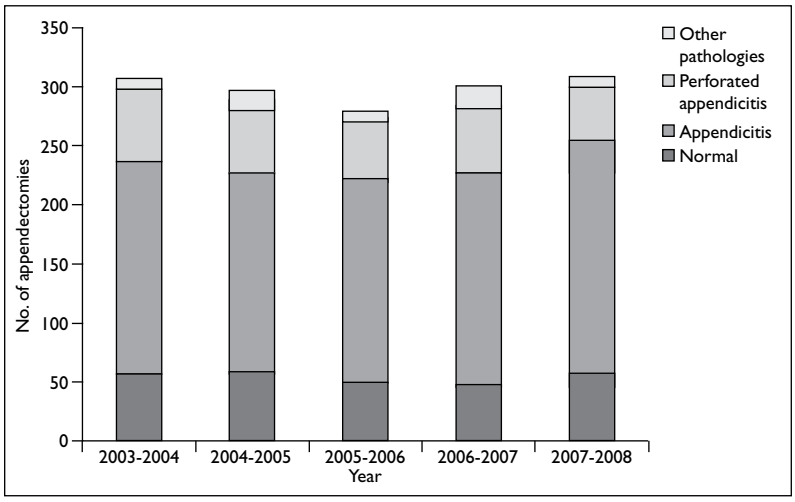

FIG 1. Number of appendectomies performed each year

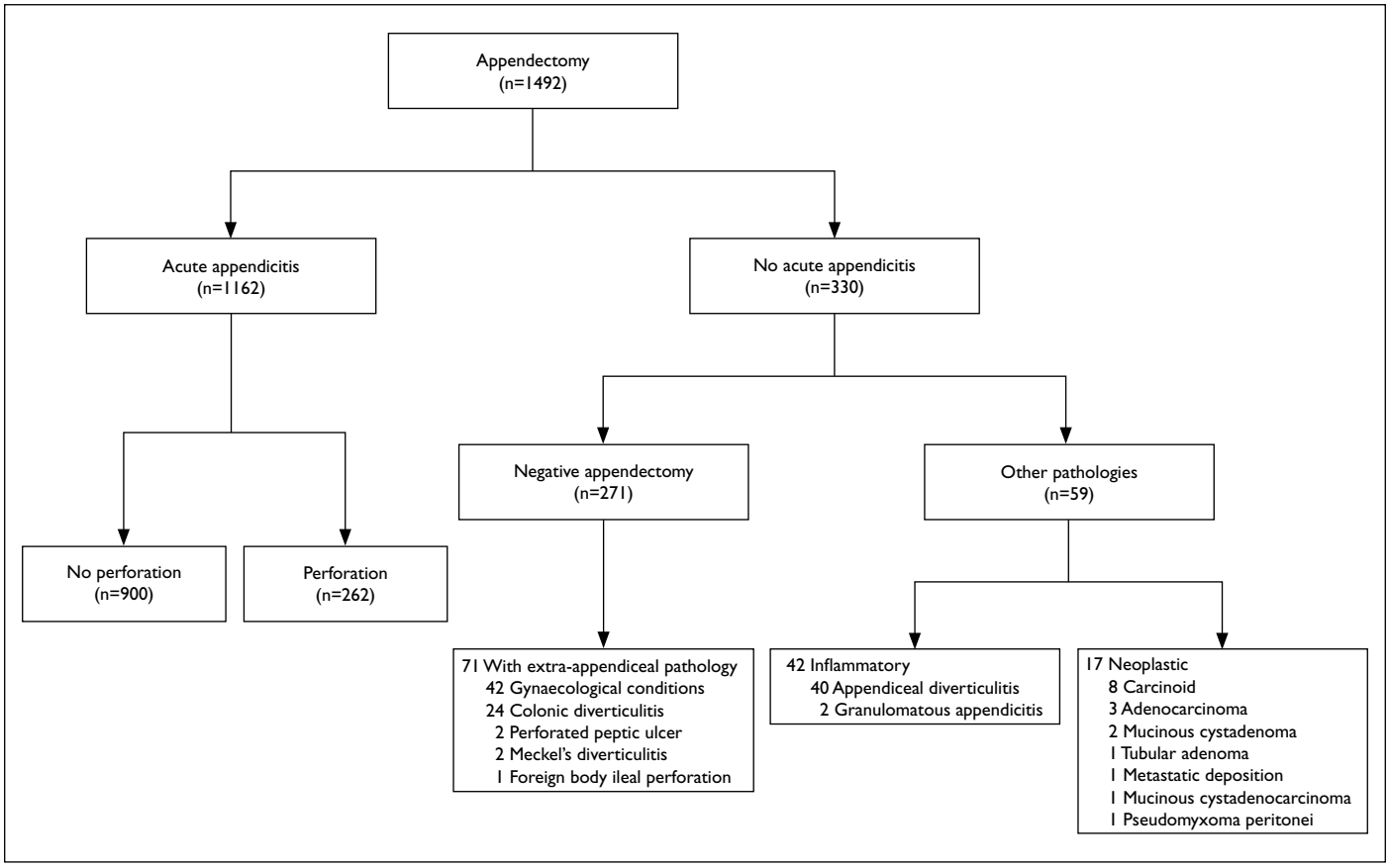

FIG 2. Breakdown of appendectomies performed

rate was 22.5% (24.8% in males vs 20.1% in females; P=0.68). When we compared the perforation rate in different age-groups, patients at the extremes of age were more likely to have a perforation (25.2% vs 16.3%; P=0.002). On performing univariate and multivariate analyses (Tables 1 and 2), patients with a normal appendix tended to have a lower mean preoperative white cell count (P<0.001). Patients with a perforated appendicitis tended to have higher body temperatures and pulse rates on admission (P=0.004 and 0.003, respectively). Preoperative imaging was not associated with a lower NAR or perforation rate (P=0.205 and 0.218, respectively). The 30-day mortality rate for patients who underwent appendectomy was 0.2%.

Appendiceal pathology other than acute appendicitis was found in 59 patients, making an overall percentage of 4.0%. The majority of these were inflammatory appendiceal lesions (42/59, 71.2%); 40 of them had appendiceal diverticulitis and two had granulomatous appendicitis. Of the 17 neoplastic appendiceal lesions, 10 were in males, and their ages ranged from 19 to 84 years, 70% were older than 50 years. The most common neoplastic appendiceal pathology was carcinoid tumour, found in eight patients (0.5% of all appendectomies), followed by adenocarcinoma (n=3) and mucinous cystadenoma (n=2). Tubular adenoma, mucinous cystadenocarcinoma, secondary adenocarcinoma deposits, and pseudomyxoma peritonei were each found in one patient.

In 271 patients with a normal appendix, extra-appendiceal pathology was found in 71 (4.8% of all appendectomies); 42 (5.5% of all female patients) had a gynaecological pathology, including: ovarian cysts, endometriosis, and pelvic inflammatory disease. In all, 24 (1.6% of patients) had colonic diverticulitis, caecal diverticulitis being the most common (21 out of 24). Perforated peptic ulcer and Meckel's diverticulitis were each found in two of the patients. One of the patients was found to have a perforation of the terminal ileum due to fish bone ingestion.

Discussion

This study showed that the incidence of acute appendicitis remained similar throughout the 5-year period, which is consistent with the study performed by Körner et al.[1] Negative appendectomy and perforation of an inflamed appendix are the two main adverse outcomes in managing suspected acute appendicitis. They are usually the result of a low operative threshold and prolonged observation, respectively. Although this is a simple logic, the decision 'to operate or not' is always a challenge even to a senior surgeon. The quoted NAR was 15 to 25%, but

TABLE 1. Univariate and multivariate analyses of different factors associated with negative appendectomy

Criteria	Negative appendectomy	Acute appendicitis and other appendiceal pathologies	P value (univariate)	P value (multivariate)
Sex (male:female)	1:1.88	1.07:1	<0.001	<0.001
White blood cells* (x 10^9/L)	12.4-13.5	14.2-14.8	<0.001	<0.001
Temperature† (ºC)	37.1-37.3	37.3-37.4	0.209	-
Pulse‡ (beats/min)	90-95	90.0-92.7	0.445	-
Duration of symptom§ (days)	2.0-2.6	2.1-2.5	0.741	-
Preoperative imaging (yes vs no)	16.6% vs 19.2%	83.4% vs 80.8%	0.205	-
Age‖	28.7% vs 11.5%	71.3% vs 88.5%	<0.001	<0.001

* Preoperative white cell count
† Body temperature upon admission
‡ Pulse rate upon admission
§ Before presentation
‖ Comparing female patients of reproductive age (11-50 years) versus non-reproductive age

TABLE 2. Univariate and multivariate analyses of different factors associated with perforation

Criteria	No perforation	Perforation	P value (univariate)	P value (multivariate)
Sex (male:female)	1:1.14	1.32:1	0.003	0.002
White blood cell* (x 10^9/L)	13.8-14.3	14.4-15.5	<0.001	0.083
Temperature† (ºC)	37.2-37.3	37.4-37.6	<0.001	0.004
Pulse‡ (beats/min)	88.8-91.4	95.6-100.6	<0.001	0.003
Duration of symptoms§ (days)	2.0-2.5	2.2-2.7	<0.001	0.599
Preoperative imaging (yes vs no)	83.2% vs 81.9%	16.8% vs 18.1%	0.218	-
Age‖	83.7% vs 74.8%	16.3% vs 25.2%	0.003	0.002

* Preoperative white cell count
† Body temperature upon admission
‡ Pulse rate upon admission
§ Before presentation
‖ Comparison made between patients of age (11-70 years) versus age (<11 or >70 years)

could be as high as 40% in female patients.[2-4] The NAR in our study was 18.2%, which was within the expected range. Since the appendix is in close proximity to the reproductive organs in females, many common gynaecological conditions like dysmenorrhoea and ovarian cyst complications can masquerade as acute appendicitis, thus accounting for their higher NAR. Patients of extreme age are more likely to have a delayed diagnosis due to atypical presentations and less efficient communication. Preoperative imaging has been advocated so as to minimise the chance of a negative appendectomy. Some studies even suggested that routine preoperative imaging could reduce the NAR,[5,6] but others were contrary.[7,8] The authors of this study do not favour the practice of 'routine' preoperative imaging, because (1) it could never replace taking a thorough history and physical examination; (2) it may overload the radiology department with abdominal pain patients, and (3) it could lead to delayed treatment and hence increased chance of perforation. We suggest preoperative imaging be offered more liberally to the two patient groups that we have discussed. Our study could not effectively demonstrate the usefulness of preoperative imaging in reducing the NAR and perforation rate, as this study did not capture patients having putative 'preoperative imaging' that were discharged without an operation. A properly designed prospective study in collaboration with radiologists to standardise imaging and reporting could be helpful. Laparoscopic appendectomy should be the standard treatment for acute appendicitis. Apart from the advantages of producing a smaller wound, these patients usually had a less severe course, a lower risk of postoperative ileus and infective complications, and enjoyed relatively shorter hospital stays. The appendectomy mortality rate in our cohort was comparable to that in a Swedish study, in which 117 424 patients were recruited and the average 30-day mortality was 0.19%.[9] In our study, all the deaths were in patients of 80 years old or older who also had multiple medical co-morbidities.

In our cohort, 9% of the patients had atypical appendicular pathology; some of whom required further clinical attention and surveillance. It is

important that surgeons have some idea of how to deal with such atypical findings. Appendiceal diverticulitis was the most common inflammatory lesion, its point prevalence of 2.7% was slightly higher than around 2% as quoted in the literature.[10-12] Many authorities consider appendiceal diverticulitis to be no different from ordinary appendicitis, although the former usually affects older subjects. In our series, the mean age of patients with appendiceal diverticulitis was 10 years older than those with acute appendicitis. The onset of abdominal pain could be more sub-acute and intermittent,[13] and the respective perforation and mortality rates are 4 and 30 times more than those in the acute appendicitis.[12] Granulomatous appendicitis was another inflammatory lesion encountered in our series but is far less common, though the quoted point prevalence in western countries is 2%.[14,15] Causes of granulomatous appendicitis include infection by fungi, *Yersinia pseudotuberculosis*, mycobacterium tuberculosis, parasites, Crohn's disease, foreign body reactions, and sarcoidosis. After exclusion of these causes, idiopathic granulomatous appendicitis is a benign disease. However, follow-up is suggested because the differentiation of appendiceal Crohn's and granulomatous appendicitis is difficult, and there are reports that granulomatous appendicitis may be a forerunner of Crohn's disease.[16-18]

Concerning the neoplastic appendiceal lesions, carcinoid tumour was the most common and contributed to 0.5% of the cases in our study, which is also comparable to the rate quoted in the literature (0.3-0.9%).[19,20] Most studies agree that appendectomy is the only required procedure in patients with carcinoid tumours of less than 2 cm in diameter, as they generally have a favourable prognosis. Right hemicolectomy should be considered if the tumour diameter exceeds 2 cm, there is evidence of mesoappendiceal extension and lymphovascular permeation, the tumour involves the base of appendix or caecum with positive margins, there is a high mitotic index and Ki67 levels, or goblet cell carcinoid is present.[19,21,22] Nonetheless, laparotomy and right hemicolectomy are procedures associated with morbidity. Surgeons should therefore have a higher operative threshold for patients with advanced age and high operative risks in view of the low recurrence rate, and the smoldering nature of carcinoid disease.[23,24]

In cases of appendiceal carcinoma and other non-carcinoid tumours, oncological resection with right hemicolectomy is the treatment of choice. Regular colonoscopic surveillance for metachronous tumour is recommended in patients with primary neoplastic appendiceal diseases, including carcinoid tumours.[20,25] Concerning the pseudomyxoma peritonei, it is a rare condition secondary to the release of mucinous tumour cells from the appendix, usually by means of a ruptured mucocele.[26] As described by Sugarbaker,[27] its treatment includes radical peritonectomy and hyperthermic intra-peritoneal chemotherapy.

Conclusions

Appendectomy continues to be a very common surgical procedure. We suggest a more liberal utilisation of preoperative imaging in females of reproductive age, and patients at the extreme age. Long-term follow-up should be offered to patients with granulomatous appendicitis and neoplastic appendiceal diseases, as there may be a potential for development of Crohn's disease and carcinoma,

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