Histopathological features of incidental appendectomy specimens obtained from living liver donors

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ABSTRACT

Background/Aims: To determine the histopathological features of incidental appendectomy specimens obtained from living liver donors (LLDs)

Materials and Methods: Between September 2005 and November 2018, 1910 LLDs underwent living donor hepatectomy at our institute. Incidental appendectomy together with living donor hepatectomy (LDH) was performed in 170 LLDs. The decision for incidental appendectomy was made by experienced gastrointestinal surgeons. Histopathological features of the appendectomy specimens were analyzed by two pathologists, and the following parameters were retrospectively evaluated: age, sex, appendix length (mm), appendix width (mm), presence of appendicitis, and unusual histopathological findings.

Results: Histopathological findings from 97 male and 73 female LLDs aged between 18 and 64 (median: 30) years were retrospectively examined. The length of the appendix vermiformis ranged from 25 to 120 (median: 70) mm, whereas its width ranged from 4 to 13 (median: 6) mm. The following histopathological findings were observed: normal appendix vermiformis (n=137), fibrous obliteration (n=13), acute appendicitis (n=5), enterobius vermicularis (n=4), lymphoid hyperplasia (n=4), low-grade appendiceal mucinous neoplasm (n=2), mucinous cystadenoma (n=1), grade 1 neuroendocrine tumor (n=1), hyperplastic polyp (n=1), enterobius vermicularis with fibrous obliteration (n=1), and acute appendicitis with eosinophilic infiltration (n=1).

Conclusion: This study showed that a careful inspection of the abdominal cavity was useful, and appendectomy should be performed when required. In addition, even if the macroscopic appearance of the appendectomy specimens is normal, histopathological evaluations facilitate an early diagnosis of numerous unusual appendiceal diseases.

Keywords: Living liver donor, living donor hepatectomy, incidental appendectomy, histopathological features

INTRODUCTION

Appendectomy is the most frequent emergency abdominal surgery performed worldwide, and acute appendicitis is the most common indication for appendectomy (1, 2). Acute appendicitis is an inflammatory condition that is caused by the spread of an inflammatory process in the mucosal layer of the appendix vermiformis toward the serosa (1, 2). The main triggering factor that initiates this inflammatory process is luminal obstruction due to various reasons. The most frequent etiopathogenic factors underlying such luminal obstruction are lymphoid hyperplasia in children and fecalith in adults. In addition to these common causes, numerous unusual factors have been identified that can cause acute appendicitis or mimic acute appendicitis findings without any histopathological changes (1, 2). The most common unusual factors that have been histopathologically detected in appendectomy specimens are as follows: fibrous obliteration, eosinophilic infiltration, parasitic infestations, actinomycosis, tuberculosis, Crohn's disease, endometriosis, diverticulitis, foreign body, benign tumors (mucinous cystadenoma, mucocele, and polyps), and malignant tumors (neuroendocrine tumor, adenocarcinoid tumor, gastrointestinal stromal tumor, adenocarcinoma, mucinous cystadenocarcinoma, lymphoma, and leukemia) (1-4).

Appendectomy can be terminologically divided into four groups according to the timing of appearance and indication of surgery: emergency (standard) appendectomy, elective (interval) appendectomy, prophylactic appendectomy, and incidental appendectomy. Incidental appendectomy is defined as the resection of the appendix vermiformis due to various reasons that might occur during abdominopelvic surgery (5). Debates regarding incidental appendectomy have been ongoing during the last century, but no clear consensus has been reached until now. The most important topic of debate is wheth-

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er appendectomy is necessary during elective abdominopelvic surgery or not (5). Another important topic related to incidental appendectomy is the histopathological changes in the appendectomy specimen. The aim of this study was to determine the histopathological changes in incidental appendectomy specimens obtained from living liver donors (LLD).

MATERIALS AND METHODS

Between September 2005 and November 2018, 1910 LLD candidates underwent living donor hepatectomy (LDH) at the Inonu University Liver Transplant Institute. Incidental appendectomy together with LDH was performed in 170 (8.9%) LLDs. The LDH technique applied in our transplant institute has been detailed in earlier studies. A J-shaped incision, also known as the reverse L, was used for laparotomy for all the LLD candidates. The decision regarding incidental appendectomy was based on the clinical prediction of surgeons that were experienced in gastrointestinal surgery. Surgeons decided upon appendectomy based on one or more of the following reasons: (i) increased risk of appendicitis after major abdominal surgery; (ii) risk of complications as well as an issue in which the duration of surgery may increase when appendectomy is performed in cases with a history of major abdominal surgery; (iii) lateral end of the J-shaped incision used for LDH is very close to the ileocecal region in some patients, thereby increasing the risk of manipulation of the appendix vermiformis during abdominal wall retraction; (iv) palpable fecalith within the appendix vermiformis; and (v) intraoperative findings suggestive of acute appendicitis, such as increase in size of the appendix, wall edema, hyperemia, and erectile appendix vermiformis (5). After obtaining the approval from the Inonu University Rectorate Ethics Committee (approval no.: 2019/01-5), the patients' demographic characteristics and pathology reports were retrospectively reviewed. The following parameters were evaluated for this study: age (years), sex (male or female), appendix length (mm), appendix width (mm), presence of appendicitis, and unusual histopathological findings.

The histopathological features of the appendectomy specimens were reevaluated by two pathologists. Briefly, appendix vermiformis specimens were fixed in 10% formalin solution. Routinely prepared paraffin-embedded tissues were sliced (thickness: 4 μm) and stained with hematoxylin–eosin (H&E) before examination under a light microscope. The diagnosis of a carcinoid tumor was made based on the presence of neuroendocrine cells and staining of these cells with neuroendocrine markers, such as synaptophysin, chromogranin A, and neuron-specific enolase. Ki-67 (MIB-1) is a proliferation marker and can be used to determine the degree of tumor. Enterobius vermicularis and mucinous neoplasms of the appendix vermiformis are usually diagnosed with H&E staining.

RESULTS

Histopathological findings from 97 (57.1%) male and 73 (42.9%) female patients aged between 18 and 64 (mean±SD: 32.3±10.4; median: 30) years were retrospectively examined. The length of the appendix vermiformis ranged from 25 to 120 (mean±SD: 69.4±18; median: 70) mm, whereas the width of the appendix vermiformis ranged from 4 to 13 (mean±SD: 6.4±1.7; median: 6) mm.

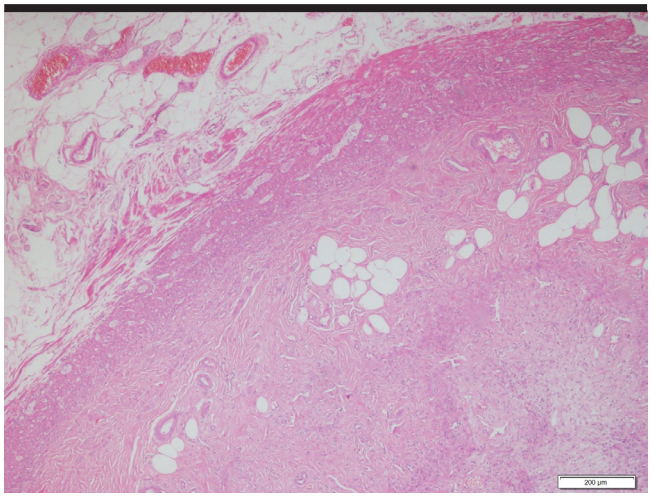

Figure 1. Fibrous obliteration of appendix vermiformis (H&E 40×).

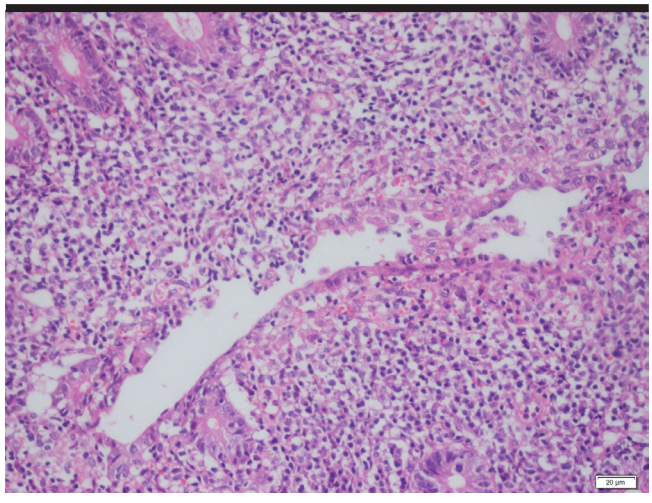

Figure 2. Early acute appendicitis findings (H&E 200×).

The age of male patients ranged from 19 to 64 (mean±SD: 30.8±9; median: 30) years, whereas the age of female patients ranged from 18 to 63 (mean±SD: 34.3±11.6; median: 32) years (p=0.059). The length of the appendix vermiformis obtained from male patients ranged from 35 to 120 (mean±SD: 72.8±17.2; median: 70) mm, whereas the length of the appendix vermiformis obtained from female patients ranged from 25 to 105 (mean±SD: 64.9±18; median: 67) mm (p=0.010). The width of the appendix vermiformis obtained from male patients ranged from 4 to 13 (mean±SD: 6.6±1.7; median: 6) mm, whereas the width of the appendix vermiformis obtained from female patients ranged from 4 to 13 (mean±SD: 6.2±1.7; median: 6) mm (p=0.104).

The histopathological findings were as follows: normal appendix vermiformis (n=137; 80.6%), fibrous obliteration (n=13; 7.6%), acute appendicitis (n=5; 2.9%), enterobius vermicularis (n=4; 2.4%), lymphoid hyperplasia (n=4; 2.4%), low-grade appendiceal mucinous neoplasm (n=2; 1.2%), mucinous cystadenoma (n=1; 0.6%), grade 1 neuroendocrine tumor (n=1; 0.6%), hyperplastic polyp (n=1; 0.6%), enterobius vermicularis + fibrous obliteration (n=1; 0.6%), and acute appendicitis with eosinophilic infiltration (n=1; 0.6%) (Figures 1-7). There was no leakage in the appendix stump in any patient during the follow-up period. In addition, relaparotomy due to incidental appendectomy was not required in any patient. Demographic and histopathological characteristics of 170 LLDs who

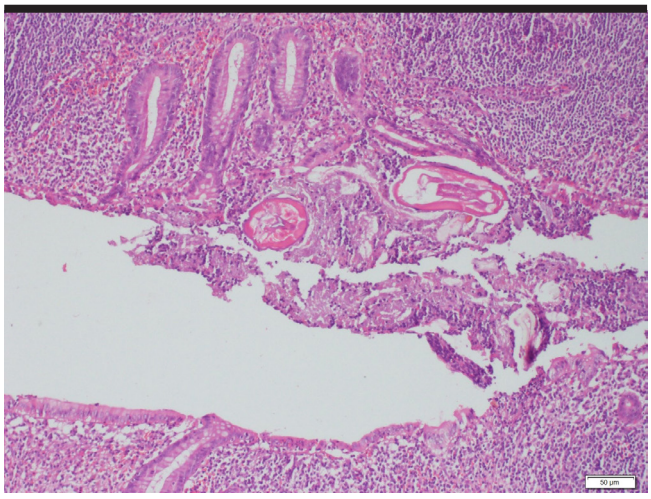

Figure 3. Enterobius vermicularis in the appendix vermiformis (H&E 100×).

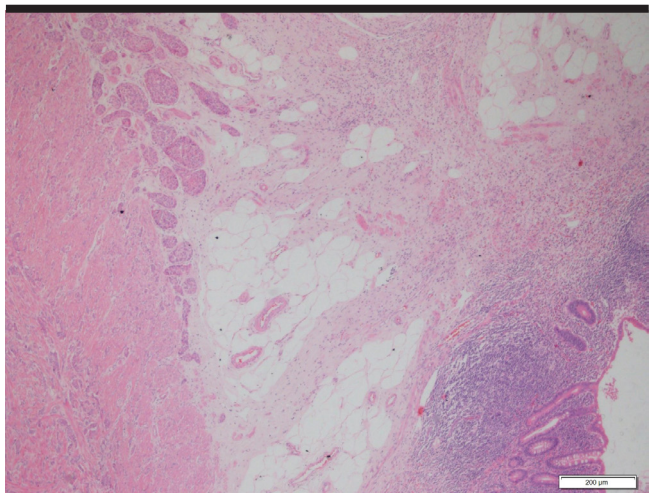

Figure 5. Carcinoid tumor island infiltrating the submucosa and muscle (H&E 40×).

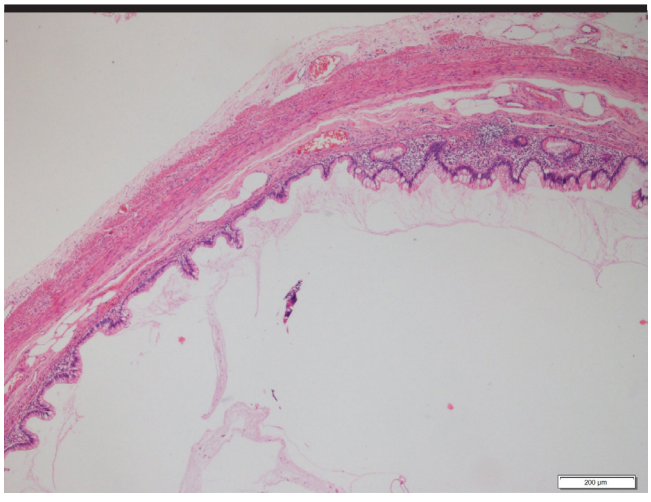

Figure 4. Low-grade mucinous neoplasia in the appendix vermiformis (H&E 40×).

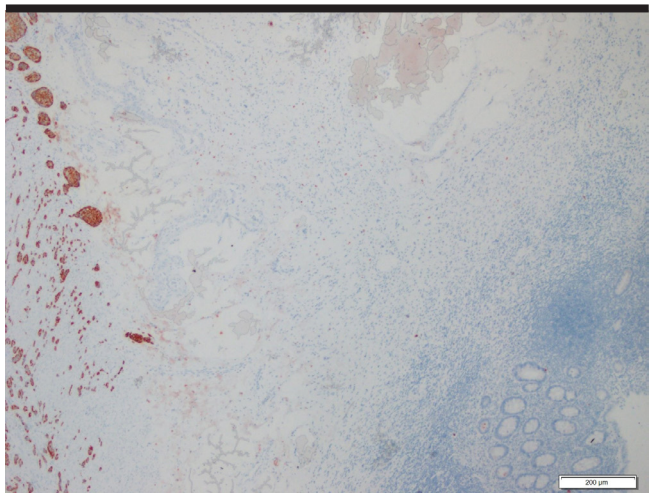

Figure 6. Positive staining with anti-chromogranin A antibody in carcinoid tumor cells (CgA 40×).

underwent incidental appendectomy are summarized in Table 1

DISCUSSION

Liver grafts needed for liver transplantations are mostly provided by LLDs in numerous Asian countries, including Turkey. LDH is one of the most important surgeries involving the abdominal cavity, and incisions used in this surgery are the right subcostal incision, chevron incision, Mercedes incision, J-shaped incision, reverse L-shaped incision, and midline incision. These gross incisions allow surgeons to perform easy maneuvers in the right upper quadrant; however, depending on the size of the incision, several complications, such as postoperative pain, adhesions, intestinal obstructions secondary to adhesions, and incisional hernia, may develop. It is not always easy to reach the abdominal cavity without injuring hollow viscus organs during laparotomy due to adhesions that are likely to occur in patients undergoing a major abdominal surgery, such as LDH. Therefore, relaparotomy leads to prolonged operation time and increases the risk of abdominal organ injury when compared with primary laparotomy.

Given both these realities and one or several of our incidental appendectomy indications specified in the Methodology section, some of our LDH patients underwent incidental appendectomy in the same session. Evidently, the lifetime risk of a true acute appendicitis attack ranges between 5% and 20% (male: 8.6%; female: 6.9%) (5-8). On the contrary, the lifetime risk of appendectomy surgery in men and women has been shown to be 12% and 23%, respectively (5, 8). These data indicate that the lifetime risk of acute appendicitis is exceptionally high and that humans undergo appendectomy for reasons other than acute appendicitis. Negative and incidental appendectomy operations may account for the discrepancy between true acute appendicitis risk and appendectomy risk.

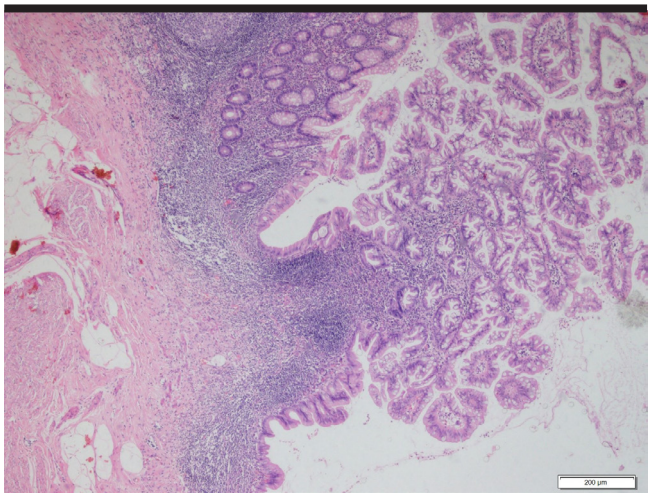

Figure 7. Hyperplastic polyp in the mucosa of appendix vermiformis (H&E 40×).

The first scientific study regarding incidental appendectomy was performed by Kelly in 1902 as a questionnaire study for American surgeons (5, 9). Despite more than

Table 1. Demographic and histopathological characteristics of 170 living liver donors underwent incidental appendectomy.

Patients' characteristics (n=170)	Results	%
Age (years)		
Mean±SD	32.3±10.3	
Median	30	
Min-Max	18-64	
IQR	14	
Sex		
Male	97	57.1
Female	73	42.9
Length of the Appendix Vermiformis (mm)		
Mean±SD	69.4±17.9	
Median	70	
Min-Max	25-120	
IQR	20	
Diameter of the Appendix Vermiformis (mm)		
Mean±SD	6.5±1.7	
Median	6	
Min-Max	4-13	
IQR	2	
Histopathological features		
Appendix vermiformis	137	80.6
Fibrous obliteration	13	7.6
Acute Appendicitis	5	2.9
Enterobius Vermicularis	4	2.4
Lymphoid Hyperplasia	4	2.4
Low Grade Mucinous Neoplasm	2	1.2
Mucinous cystadenoma	1	0.6
Grade I Neuroendocrine Tumor	1	0.6
Hyperplastic polyp	1	0.6
Enterobius vermicularis+ Fibrous obliteration	1	0.6
Acute appendicitis+ Eosinophilic infiltration	1	0.6

a hundred years of debate, incidental appendectomy is performed during many abdominopelvic surgical procedures. The American College of Obstetricians and Gynecologists recommends incidental appendectomy in the following situations: women under 35 years old who need to undergo pelvic surgery; patients undergoing open or laparoscopic abdominal exploration under the differential diagnosis of chronic pelvic pain and endometriosis; patients undergoing abdominopelvic surgery with a potential of causing adhesions; patients with developmental anomalies, which prevent them from expressing their symptoms; and to protect patients undergoing laparotomy from future elective appendectomy risk (5, 10-12). In familial Mediterranean fever disease that mimics the signs and symptoms of acute appendicitis, incidental appendectomy is recommended during diagnostic abdominal exploration, even when the appendix appears to be macroscopically normal (13). In contrast, a consensus has been reached not to perform appendectomy in the absence of any absolute indications in patients undergoing chemo-/radiotherapy, patients with Crohn's disease, patients with intestinal tuberculosis, unstable patients, and patients using artificial grafts.

Researchers in favor of incidental appendectomy suggest that adhesions that develop after a major abdominopelvic surgery increase both complication risk and operation time; therefore, considering the lifetime risk of acute appendicitis, they have hypothesized that incidental appendectomy—associated with a short operation time, very low complication risk, and does not require additional anesthesia—would be beneficial. Opponents of incidental appendectomy suggest that during this procedure, feces contaminate the abdominal cavity during the removal of an organ that is in direct communication with the colonic lumen, thereby causing infectious complications (5).

In the present study, rather than discussing the indications for incidental appendectomy, we aimed to determine histopathological changes in the appendectomy specimens obtained from healthy individuals undergoing incidental appendectomy, as well as to examine whether these changes were similar to those reported by other studies in the medical literature or not. The full text from 16 articles regarding the histopathological features of incidental appendectomy specimens were investigated further (summarized in Table 2) (14-29). An analysis of the histopathological features of these appendectomy specimens revealed appendix vermiformis (normal appendix) in 22.6%-89.2% patients; acute appendicitis, 0%-9.2% patients; endometriosis, 0%-37% patients; and various appendiceal tumors, 0%-4.2% patients. The main reason for the fairly lower rates of appendix vermiformis in certain studies is the lack of a common termi-

Table 2. Histopathological view of some published article on incidental appendectomy.

References	Year	Indication for Surgery	IA	Appendix Verm.	AA	Endomet.	Malign tumor
Huttenbrink	2018	Radical Prostatectomy	53	62.3	5.6	0	3.7
Choksuwattan.	2017	Postopartum Sterilization	139	89.2	5.7	0.7	0
Tartaglia	2016	Lower Quadrant Pain	164	24	5	0	2
Riberio	2015	Infertility+ Pelvic Pain	109	26.6	0.9	27.6	0.9
Jocko	2013	Pelvic mass+ Pelvic Pain+ Endomet.	71	41	4	37	4.2
Exner	2012	Colorectal Cancer	380	22.6	9.2	0	1
Lee	2011	Endomet.	172	69.8	6.1	9.3	2.3
Song	2009	Infertility+ Pelvic Pain+ Endomet.	772	22.7	4.3	2.2	0
Wie	2008	Endomet.	106	65.1	5.6	13.2	2.8
Akl	2008	Gynecological Surgery	107	69.1	0.9	3.7	2.8
Albright	2007	Benign or Malign Intestinal Surgery	341	75.1	0	0.3	2.4
O'Hanlan	2007	Pelvic pain+ Future Appendicitis	257	52	0	4	1.1
Salom	2003	Abdominal Hysterectomy	100	69	1	1	0
Greason	1998	Lower Quadrant Pain	44	81.8	4.5	0	0
Lynch	1997	Gynecological Surgery	130	29	0	8.5	0
Lowery	1962	Cholecystectomy	116	71.6	3.4	0	1.7

IA: Incidental appendectomy; AA: Acute appendicitis; Endomet: Endometriosis; Verm: Vermiformis

nology between pathologists working at different clinics. For instance, some authors have used terms such as catarrhal appendicitis and chronic appendicitis, which are rarely used today. In studies where endometriosis could not be detected, the prevalence of appendix vermiformis was over 70%. In our cohort, the rate of appendix vermiformis was 80.6%.

Another important finding that needs to be considered is the high endometriosis rate in incidental appendectomy specimens. Our literature analysis showed that the rate of appendiceal endometriosis ranged between 2.2% and 37% in patients undergoing surgery for pelvic pain and a preliminary diagnosis of infertility, while it ranges between 0% and 0.3% in those undergoing incidental appendectomy during gastrointestinal system or prostate surgery. In contrast, the rate of endometriosis ranges between 0.05% and 0.15% in patients undergoing appendectomy due to the presumed diagnosis of acute appendicitis (1, 4). Higher appendiceal endometriosis rates are a reasonable ground for gynecologists to recommend routine incidental appendectomy for patients undergoing exploration for pelvic pain and infertility.

The rate of appendiceal cancer in incidental appendectomy is one of the points to be considered. The rates of appendiceal tumors among patients undergoing appendectomy for the preliminary diagnosis of acute appendicitis range between 0.2% and 0.87% (1-3). In contrast, our literature scan revealed that half the available studies have reported that cancer prevalence ranged between 2% and 4.2%. In our cohort, the appendiceal tumor rate was 0.6%. One of the most important indications of incidental appendectomy is the future risk of malignancy. Considering this high prevalence of cancer in the incidental appendectomy specimens, a worthy question can be raised: should we perform incidental appendectomy for all the patients undergoing abdominal exploration to prevent future malignancy risk? Although a limited number of authors have advocated that it should be performed, a consensus has not been reached (12). Considering the risk of future malignancy, we favor incidental appendectomy, but large-scale studies are clearly required.

Apart from the important issues mentioned above, many rare histopathological findings may be observed in incidental appendectomy specimens, most notably fibrous obliteration and parasitic diseases. The fibrous obliteration and enterobius vermicularis rates observed in this study are similar to those detected in patients undergoing appendectomy due to acute appendicitis.

This study has a different aspect from other studies with respect to studies regarding incidental appendectomy in the literature. In all the studies regarding incidental appendectomy that have been published so far, patients have been operated for surgical, urological, or gynecological conditions, during which incidental appendectomy has been performed. Nevertheless, patients in our study were completely healthy and agreed to undergo laparotomy to donate a part of their liver to their relatives. Hence, the histopathological findings of appendectomy specimens obtained from them represent the appendix structure of healthy individuals within the general population.

In summary, in the present study, we do not support the idea that everyone undergoing laparotomy should be operated for incidental appendectomy. We merely recommend that the abdominal cavity should be gently examined, and incidental appendectomy should be performed—if necessary—in patients undergoing laparotomy for any reason. Despite many contrary views in the literature, surgeons, particularly gynecologists, continue to perform incidental appendectomy due to the various reasons specified above.

Ethics Committee Approval: Ethical approval was obtained from Inonu University institutional review board for non-interventional studies (Approval No:2019/01-5).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.A., C.K., B.S.; Design - S.A., C.K., B.S.; Supervision – S.A., S.Y., Resources - S.A., C.K.; Materials - C.K., B.S., E.S., M.O.; Data Collection and/or Processing- C.K., B.S., E.S., M.O.; Analysis and/or Interpretation - B.B., A.J.W., A.G.; Literature Search – S.A., C.K.; Wiritng Manuscript – S.A.; Critical Review – S.A., S.Y.

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