



Incidence of malignancy in adrenal nodules detected on staging CTs of patients with potentially resectable colorectal cancer

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Abstract

Objective To measure the prevalence of adrenal nodules detected on staging CT in patients with resectable colorectal cancer, and the proportion of patients with malignant nodules among them.

Methods This retrospective study included 6474 patients (median age, 65; interquartile range, 56–73; 3902 men) who underwent staging CT for colorectal cancer between May 2003 and December 2018. The patients had potentially resectable colorectal cancer, including resectable hepatic or pulmonary metastases. Through retrospective CT image review, patients with adrenal nodules were identified for the prevalence of adrenal nodule. Among patients with adrenal nodules, *per-patient* proportions of malignant nodules, adrenal metastasis from colorectal cancer, and additional adrenal examinations (biopsy or imaging tests) were measured. A secondary analysis was performed using data from the official CT reports.

Results The prevalence of adrenal nodules was 5.6% (363 of 6474; 95% CI: 5.1, 6.2). The proportions of malignant nodules and adrenal metastasis from colorectal cancer were 0.8% (3 of 363; 0.2, 2.4) and 0.3% (1 of 363; 0.0, 1.5), respectively. 6.1% (22 of 363; 3.8, 9.0) of the patients underwent additional adrenal examination. According to official CT reports, the prevalence of adrenal nodules and proportions of malignant nodules, adrenal metastasis from colorectal cancer, and additional adrenal examination were 1.9% (125 of 6474; 1.6, 2.3), 1.6% (2 of 125; 0.2, 5.7), 0% (0 of 125; 0.0, 2.9), and 10.4% (1 of 125; 5.7, 17.1), respectively.

Conclusion Adrenal nodules detected in staging CTs in patients with otherwise resectable colorectal cancers are rarely malignant.

Key Points

- Among 6474 patients who underwent staging CT and had potentially resectable colorectal cancer, 363 had adrenal nodules (≥ 10 mm) detected in retrospective CT image review.
- Three out of the 363 patients with adrenal nodules detected on staging CT had malignant adrenal nodules, one of whom had metastasis from colorectal cancer.

Keywords Adrenal glands · Tomography, x-ray computed · Prevalence

Abbreviations

CI Confidence interval

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Introduction

Colorectal cancer is the third most commonly diagnosed cancer globally with an estimated 916,000 deaths in 2020 [1]. Curative resection (i.e., surgery or endoscopic resection) is the treatment of choice for patients without evidence of distant metastasis and for selected patients with hepatic or pulmonary metastases that can be excised radically [2, 3]. For staging of colorectal cancer and subsequent determination of treatment strategy, computed tomography (CT) of abdomen and pelvis is routinely performed, and adrenal nodules are detected incidentally in 2–4% of cases [4, 5]. Characterization of such adrenal nodules during staging workup is particularly important for patients who are otherwise candidates for curative resection.

While there is no specific guideline for the management of an adrenal nodule detected during staging workup for colorectal cancer, all general guidelines on adrenal incidentalomas [6–11] recommend some form of additional imaging tests for initial nodule characterization. Since adrenal incidentalomas are usually detected on single-phase CTs acquired in the portal-venous phase where characterization of the nodules is difficult, four of the existing guidelines [7–9, 11] specifically recommend additional non-contrast CT. One other guideline [1] recommends additional multi-phase adrenal CT, while the remaining one guideline [2] does not specify the form of additional imaging. However, the guidelines also acknowledge the fact that differentiation of benign vs. malignant adrenal nodules may be inconclusive even after additional imaging tests, since up to one-third of adrenocortical adenomas are lipid poor [12], and there is a considerable overlap in washout patterns of benign and malignant nodules [12–15]. How the nodules that are judged as not definitely malignant on initial assessment should be followed up is yet another question, with substantial heterogeneity among the guidelines.

Although there is limited supporting data [16], there is a prevailing consensus among clinicians that solitary adrenal metastasis from colorectal cancer is very rare. If this presumption turns out to be true, routinely applying the guidelines recommending additional adrenal imaging at the time of staging workup may incur unnecessary costs and increase patient anxiety as well as delay definitive treatment without a clinically meaningful diagnostic yield, particularly in patients with colorectal cancer without distant metastasis. On the other hand, there is no previous study concerning whether the presence of an adrenal nodule should alter the management in patients with resectable hepatic or pulmonary metastasis.

In this study, we aimed to measure the prevalence of adrenal nodule among patients who undergo staging CT and have potentially resectable colorectal cancer, and the proportion of malignant nodule among them. Such knowledge would

provide the basis for refining the guidelines on managing patients with adrenal nodules detected during staging workup for colorectal cancer.

Materials and methods

Study setting

The institutional review board approved this retrospective observational study and waived patient informed consent. The study took place in a tertiary hospital in South Korea, with study period from May 2003 to December 2018. Weekly multidisciplinary meetings were held in which colorectal cases were discussed, particularly regarding tumor resectability. Our practice was generally in line with the guidelines by National Comprehensive Cancer Network [17]. We wrote this report according to a relevant reporting guideline [18]. The term colorectal cancer in our study refers collectively to adenocarcinoma and other histopathological entities that share the 8th American Joint Committee on Cancer (AJCC) TNM staging system (e.g., neuroendocrine carcinoma), except for adenocarcinoma in situ. Outcome measures in this study, along with the adjudication criteria used for the reference standard, were adapted from our previous study on adrenal nodules detected in patients with potentially resectable gastric cancer [19].

Patients

Our target population was patients with potentially resectable colorectal cancer. To capture a study sample representative of the target population, we identified all patients meeting either of two criteria during the study period (Fig. 1). First, we identified patients with endoscopic biopsy-confirmed colorectal cancer by searching the pathology database of colorectal specimens from endoscopic biopsy or endoscopic resection. In case a specimen was so poorly differentiated that the pathologist could not decide whether it was carcinoma or other entity such as lymphoma, the patient was included as he or she was usually considered for surgical resection under working diagnosis of carcinoma. Second, we identified patients with clinically suspected colorectal cancer who underwent surgery without endoscopic confirmation. This was because some patients with CT findings highly suggestive of colorectal cancer underwent surgery without endoscopic confirmation due to risks of perforation. To identify those patients, we searched the hospital database using relevant International Statistical Classification of Diseases and Related Health Problems (ICD) codes. This gave a baseline sample of 8845 patients.

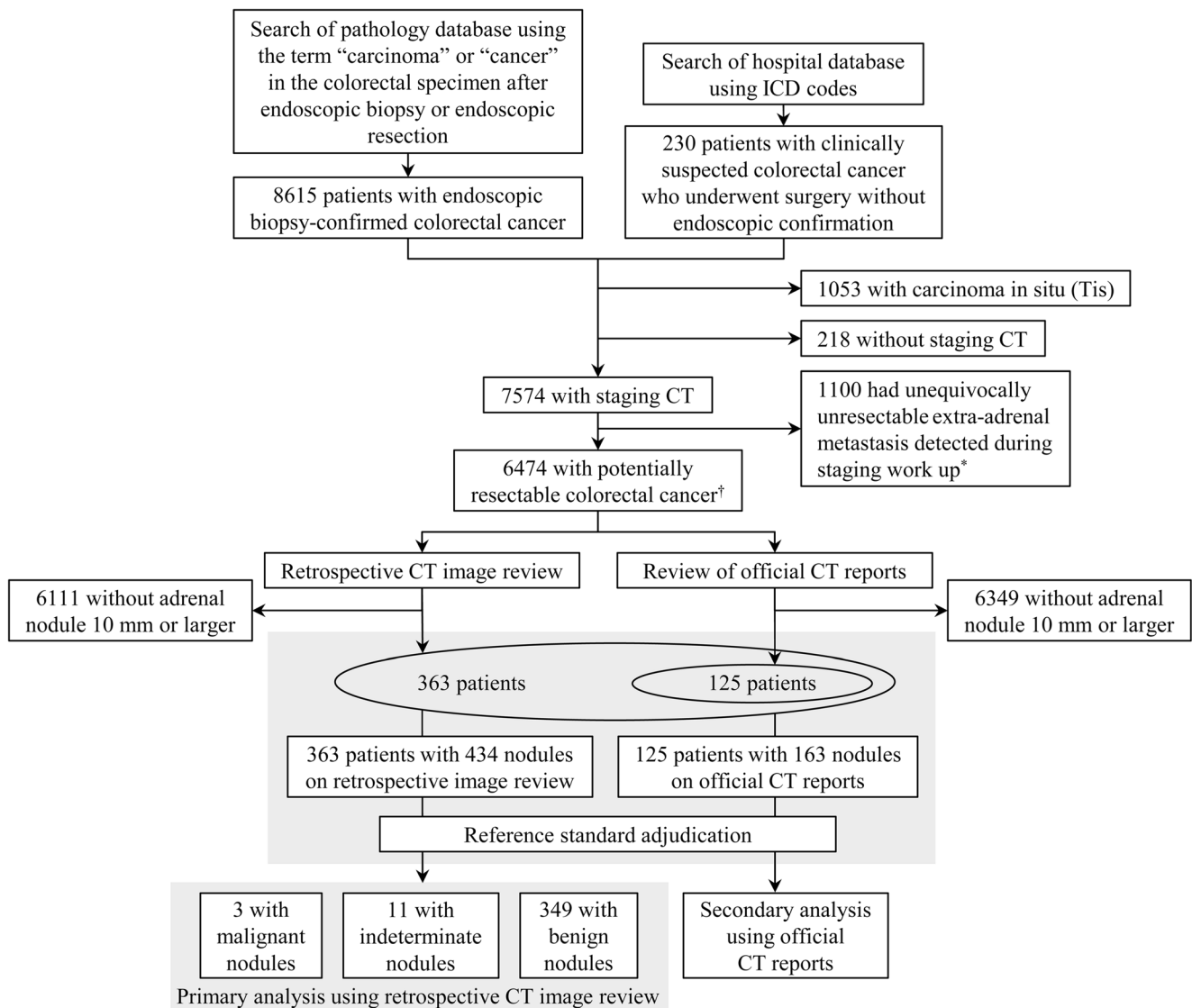


Fig. 1 Patient flow. Unless otherwise specified, data are the numbers of patients. *At the time of staging CT. †Including cancer with hepatic and pulmonary metastases that were considered resectable in

multidisciplinary conferences. *ICD*, International Statistical Classification of Diseases and Related Health Problems

We then excluded 1053 patients with carcinoma in situ, and 218 who did not undergo staging CT of the abdomen and pelvis, defined as that performed within 3 months before any definitive treatment (i.e., surgery or chemotherapy) of colorectal cancer, or within 3 months before or after endoscopic biopsy or resection. We further excluded 1100 patients having unresectable colorectal cancer at the time of staging CT, for whom adrenal nodule characterization would hardly alter patient disposition. Patients with hepatic or pulmonary metastases that were considered to be resectable via surgical resection or local ablation at the time of staging in multidisciplinary conferences were included in the patient sample. Those with rectal cancer who underwent neoadjuvant concurrent chemoradiotherapy (CCRT) with curative intention were

also included. Thus, our sample finally included 6474 patients with potentially resectable colorectal cancer.

CT protocol and follow-up

The majority of patients ($n = 5342$) underwent staging CT in our hospital, while 1132 patients underwent CT elsewhere. Most of the patients underwent multipurpose single-phase CT in portal-venous phase (Supplementary Table 1); 1451 patients underwent CT colonography (which included both pre-contrast and contrast-enhanced portal-venous phases); and 165 patients underwent CTs using various other protocols including kidney and bladder CT or CT angiography. We used various CT machines

with 16–256 channels. Image thickness was typically 4 or 5 mm. Intravenous contrast (either 350 mg/ml or 400 mg/ml, injected typically at 3 cc/s) was used in all patients except for eight, for whom positron emission tomography and/or liver MRI were used additionally. Automatic dose modulation was used for CTs performed in our hospital (Supplementary Table 1).

For imaging follow-up for colorectal cancers, clinicians in our center typically followed the guidelines by National Comprehensive Cancer Network [17], where abdomen and pelvis CTs were recommended every 6 to 12 months for 5 years in patients with stage II or III cancers, and every 3 to 6 months for the first 2 years and then every 6 months for another 3 years for those with stage IV cancers. Imaging follow-up for stage I colon cancer was determined at the discretion of the primary physician.

Identification of patients with adrenal nodules

We defined “adrenal nodule” as a focal adrenal lesion or thickening of 10 mm or larger. We used the 10-mm threshold according to guidelines [6, 20] used for workup of adrenal nodules 1 cm or larger. Since 10 mm is at the upper range of normal adrenal thickness [21], using a lower threshold would have caused too many false-positives.

For the primary analysis, we identified patients with adrenal nodules via a thorough retrospective CT image review of all 6474 patients, which would be the closest approximation of true prevalence. We assigned the CT studies evenly to four radiologists (J.J., W.C., Y.J.L., and Y.H.K. with experience of 6, 11, 15, 26 years) who were informed of the study purpose, and were instructed to identify nodules based on the longest length on either transverse or coronal reformatted plane. The radiologists were instructed to incline toward judging equivocal cases as positive rather than negative. In patients with CT-detected adrenal nodules, the radiologists recorded the size and laterality (i.e., right or left) and made screen captures of the nodules. For patients with more than one nodule, multiple records and screen captures were made accordingly. Diffuse thickening of the adrenal gland or conglomerated nodules with indefinable margin were counted as a single nodule.

We performed a secondary analysis by identifying patients with adrenal nodules reported on the official CT reports among the patients included in the primary analysis. For this purpose, a study coordinator reviewed the report texts containing the term “adrenal.” The official CT reports were made at the time of staging in a structured form in line with the American Joint Committee on Cancer TNM staging. The structured form included a section for incidental findings such as an adrenal abnormality.

Additional adrenal examination

Through search of electronic medical record, a study coordinator identified patients who underwent additional examination for adrenal nodule characterization. Additional examinations included percutaneous or excisional biopsy, and imaging tests (i.e., non-contrast CT, contrast-enhanced CT of a dedicated adrenal protocol, or MRI). Additional imaging tests were those that were performed within 6 months of the initial diagnosis of colorectal cancer, irrespective of regular imaging follow-up recommended for cancer evaluation. During the study period, there was no fixed internal guideline regarding additional workup for adrenal nodules detected during staging workup of colorectal cancer. Therefore, care providers on service determined the need of those tests at their discretion.

Reference standard

Patients with CT-detected adrenal nodules were subject to reference standard adjudication by consensus of two adjudicators. The adjudicators (H.Y.K. and Y.J.L., with 7 and 15 years of experience) reviewed the CT images on PACS and identified the nodules according to annotated screen captures made during the retrospective CT image review. They made the per-nodule adjudication using the predefined criteria, as detailed in the [Supplemental materials](#). All nodules were categorized as one of malignant, benign, or indeterminate nodules. Per-patient adjudication followed the results of per-nodule adjudication. A patient was counted as a malignant case if he or she had any malignant adrenal nodule. Of the patients without any malignant nodules, those who had indeterminate nodules were counted as having an incomplete reference standard. Patients with neither malignant nor indeterminate nodule were counted as benign cases.

Outcome measures

We had the following research questions. First, how many of patients with potentially resectable colorectal cancer have an adrenal nodule on staging CT (i.e., prevalence of adrenal nodule)? Second, how many of the patients with a CT-detected adrenal nodule have a malignant nodule (i.e., proportion of malignant nodule)? Prevalence of adrenal nodule would reflect the proportion of patients who would have to undergo additional adrenal imaging according to published guidelines. Proportion of malignant nodule would represent the maximal diagnostic yield of additional adrenal imaging in detecting malignant adrenal nodules, under an unrealistic assumption that the additional imaging has 100% diagnostic sensitivity. We additionally measured the proportion of patients with adrenal metastasis from colorectal cancer, and the proportion of patients who underwent additional adrenal examination, among patients with CT-detected adrenal nodules.

Statistical analyses

Two investigators planned all analyses before the data collection. A statistician performed the analyses. We calculated the proportions of the endpoints and their 95% confidence intervals (CIs). All analyses were primarily on a per-patient basis. Since we included all consecutive patients to minimize selection bias, it was inevitable that some patients had an incomplete reference standard due to lack of follow-up. We regarded these patients without a reference standard as not having malignant nodules, and instead performed a sensitivity analysis by assuming that the proportion of patients with malignant adrenal nodules in those patients was five percentage points higher than that of the patients with a complete reference standard. As stated earlier, we used the data of the retrospective CT image review for the primary analysis and added a secondary analysis using official CT reports. Because the event rates were so low, we did not perform the pre-planned subgroup analyses according to the presence of hepatic or pulmonary metastasis, other priorly or concurrently diagnosed malignancy, and cancer location.

We expected missing data to be rare and opted not to include them in the analyses. We performed all statistical analyses using STATA 14.0 (StataCorp, LLC).

Results

Patients

Of the included 6474 patients (Table 1), 3902 were men, and 2572 were women. Their median age (interquartile range [IQR]) was 65 (56–73) years. There were 2312 patients with rectal cancer, including 49 patients with synchronous colon cancer. A total of 1198 patients (18.5%) had cancer of stage pT1 (89 pN+); 841 (13.0%) had pT2 (184 pN+); 3019 (46.6%) had stage of pT3 (1512 pN+); and 579 (8.9%) had pT4 (401 pN+). A total of 309 patients (4.8%) had pathologically confirmed distant metastasis. A total of 5688 (87.9%) patients underwent surgery, and 440 patients (6.8%) underwent endoscopic resection with curative intent (Table 1).

Outcome measures

The prevalence of adrenal nodules was 5.6% (363/6474; 95% CI, 5.1–6.2%) (Table 2). The proportion of malignant nodules was 0.8% (3/363; 0.2–2.4%). In the sensitivity analysis, if the proportion of malignant nodules in the 11 patients with an incomplete reference standard was assumed as being five percentage points higher than that of the patients with a complete reference standard, the proportion of malignant nodules was 1.1% (4/363; 0.3–2.8%) (Table 2).

The proportion of adrenal metastasis from colorectal cancer was 0.3% (1/363; 0.0–1.5%). The proportion of patients who

underwent additional adrenal examination for nodule characterization was 6.1% (22/363; 3.8–9.0%): 15 patients underwent percutaneous ($n = 1$) or excisional ($n = 14$) biopsy, and 18 patients underwent additional imaging tests (Table 2). Of those 18 patients, seven underwent non-contrast CT, seven underwent adrenal CT, and four underwent adrenal MRI. All the biopsied nodules, except for one, were pathologically confirmed to be benign.

In the secondary analyses using the official CT reports, the prevalence of adrenal nodules was 1.9% (125/6474; 95% CI, 1.6–2.3%). The proportion of malignant nodules and the proportion of adrenal metastasis from colon cancer were 1.6% (2/125; 0.2–5.7%) and 0% (0/125; 0.0–2.9%), respectively. The proportion of patients who underwent additional adrenal examination was 10.4% (13/125; 5.7–17.1%).

Per-nodule adjudication results and size of nodules

A total of 434 adrenal nodules (median size [IQR], 12 mm [11–15 mm]; range, 10–74 mm) were detected in 363 patients in the retrospective CT image review. The median follow-up duration (duration between the initial and the latest CT) for the nodules that lacked pathologic confirmation was 49 months (IQR, 11–15 months). There were 6 malignant nodules in 3 patients, 16 indeterminate nodules in 11 patients with incomplete reference standard, and 412 benign nodules in 349 patients (Supplementary Table 2). There was no patient with both benign and malignant (or indeterminate) nodules. The six malignant nodules included three nodules (sizes, 12 mm, 13 mm, and 15 mm) that were adjudicated as metastases from ascending colon cancer in one patient; two nodules (12 mm and 20 mm) adjudicated as metastases from concurrent esophageal cancer in one patient; and the one remaining nodule (74 mm) adjudicated as an adrenocortical carcinoma in one patient (Supplementary Table 2, Figs. 2 and 3).

The per-nodule adjudication results for the adrenal nodules in 125 patients identified via the official CT reports are shown in Supplementary Table 3.

Discussion

In this study, we found that malignancy was rare among adrenal nodules detected on staging CTs in patients with otherwise resectable colorectal cancer. Among 6474 patients, 363 had adrenal nodules. Three out of those 363 patients (0.8%) turned out to have malignant adrenal nodules, only one of whom had metastasis from colorectal cancer. The proportion of patients who underwent additional adrenal examinations was only 6.1% in the primary analysis using retrospective image review, and 10.4% in the secondary analysis. We observed poor adherence to the existing guidelines on additional tests for adrenal incidentalomas. Our results emphasize the need to revisit those guidelines.

Table 1 Patient characteristics

Characteristics	All patients (<i>n</i> = 6474)	Patients with adrenal nodules in retrospective CT image review (<i>n</i> = 363)
Age (year)	65 (56–73)	69 (61–75)
Sex		
Women	2572 (39.7%)	114 (31.4%)
Men	3902 (60.3%)	249 (68.6%)
Body mass index (kg/m ²)	23.6 (21.6–25.8)	23.9 (21.8–26.1)
Serum carcinoembryonic antigen (mg/dl)	2.5 (1.5–5)	2.5 (1.7–5.6)
Prior or concurrent malignancy	561 (8.7%)	39 (10.7%)
Surgical or endoscopic procedure		
Endoscopic resection*	440 (6.8%)	29 (8%)
Surgery of curative intention	5688 (87.9%)	309 (85.1%)
Exploratory laparotomy or palliative surgery	37 (0.6%)	2 (0.6%)
Preoperative CCRT	601 (9.3%)	21 (5.8%)
Clinical staging ^{†,‡,§}		
cT1NanyM0	965 (14.9%)	58 (16.0%)
cT2NanyM0	675 (10.4%)	32 (8.8%)
cT3NanyM0	2888 (44.6%)	162 (44.6%)
cT4NanyM0	463 (7.2%)	31 (8.5%)
cTanyNanyM1	248 (3.8%)	14 (3.9%)
cTanyNanyMequivocal	296 (4.6%)	14 (3.9%)
Pathologic staging [§]		
pT1 or pT2, NXX	412 (6.4%)	28 (7.7%)
pT1Nany	792 (12.2%)	45 (12.4%)
pT2Nany	835 (12.9%)	39 (10.7%)
pT3Nany	3019 (46.6%)	169 (46.6%)
pT4Nany	579 (8.9%)	29 (8.0%)
pTanyNanyM1	309 (4.8%)	23 (6.3%)
Subtype based on WHO classification		
Adenocarcinoma, NOS	6167 (95.3%)	356 (98.1%)
Others	270 (4.2%)	5 (1.4%)
Differentiation based on WHO classification		
Well differentiated	1031 (15.9%)	56 (15.4%)
Moderately differentiated	4967 (76.7%)	288 (79.3%)
Poorly differentiated or undifferentiated	343 (5.3%)	16 (4.4%)
Location of cancer [¶]		
Cecum or ascending colon	1029 (15.9%)	65 (17.9%)
Transverse colon (including hepatic and splenic flexures)	537 (8.3%)	29 (8.0%)
Descending colon	258 (4%)	14 (3.9%)
Sigmoid colon	1929 (29.8%)	122 (33.6%)
Rectum	2263 (35%)	110 (30.3%)
Multiple skipped segments or straddling more than one segment	458 (7.1%)	23 (6.3%)
Multiple synchronous colorectal cancer	230 (3.6%)	17 (4.7%)

Data are *n* (%) or median (interquartile range). Data may not sum up to 100% due to missing data. All cancer staging followed the 8th American Joint Committee on Cancer TNM staging system. *Polypectomy or endoscopic mucosal resection. †Based on preoperative medical records. ‡Lower category was used if there was uncertainty in T or N classification. §The highest stage in case of multiple synchronous colorectal cancers. ||Categorized to a poorer grade in case of two or more cancers with different differentiation grades. ¶Based on pathology reports, or endoscopy reports if pathology reports were unavailable. CCRT, concurrent chemoradiotherapy; WHO, World Health Organization

Our results are in line with those from our previous study [19] that included patients with gastric cancer. In that study including 10250 patients with gastric cancer, only two out of 462 patients with adrenal nodules detected on staging CTs had malignant adrenal nodules. With such low incidence of adrenal malignancy, the vast majority of additional imaging examinations performed will be futile for the purpose of ruling out adrenal malignancy [22]. Since most patients with colorectal cancer undergo imaging follow-up for tumor surveillance or response evaluation, via which nodule stability can be ensured, additional imaging tests dedicated for adrenal evaluation at the time of staging workup may be unnecessary unless a nodule exhibits suspicious features such as a large size. To further differentiate within benign nodules, especially for diagnosing pheochromocytomas or functional adenomas, biochemical tests can be used primarily, after which additional adrenal imaging could be considered selectively. Majority of the existing guidelines [7–11] are already recommending that all patients with adrenal incidentalomas be screened for cortisol or catecholamine abnormality, although our previous study showed a very low adherence to such recommendation [19]. Once guidelines are refined, standardized reporting [23] for staging CTs may be implemented to increase awareness and adherence to the recommendations.

The discrepancy in the number of nodules detected in the retrospective image review in comparison with the official CT reports is probably because some nodules were inadvertently

overlooked, or because the radiologists intentionally dismissed the presence of a nodule based on their prior experience that small adrenal nodules are usually benign. Moreover, in the retrospective CT image review, the radiologists were instructed to identify the nodules sensitively, in order to minimize the possibility of a missed malignancy. Three metastatic nodules from colorectal cancer in a patient may not have been described in the official CT report for the same reasons.

Our study had the following strengths. First, to our knowledge, this was the first study that provided concrete epidemiologic data on the prevalence of adrenal malignancy in patients undergoing staging workup for colorectal cancer. Our patient sample of 6474 consecutive patients yielded reasonably narrow confidence intervals for the outcome measures. Even though we had already observed a very low prevalence of adrenal malignancy in patients undergoing staging workup for gastric cancer in our previous study [19], it was difficult to anticipate whether such results could be extrapolated to patients with other malignancies including colorectal cancer. Colorectal cancer differs from gastric cancer not only in its pathophysiology, but also regarding its clinical management in that surgical resection is considered more aggressively even in patients with hepatic or pulmonary metastases. Thus, unlike in our previous study [19] that excluded patients with definite distant metastasis, we included patients with resectable metastasis in this study. Second, we selected our patient sample with a strict intention-to-diagnose principle, distinguished from a convenient sampling

Table 2 Outcome measures

Outcome measures*	Primary analysis using retrospective CT image review data	Secondary analysis using official CT reports
Prevalence of adrenal nodule	5.6% (5.1%, 6.2%) [363/6474]	1.9% (1.6%, 2.3%) [125/6474]
Proportion of malignant nodule	0.8% (0.2%, 2.4%) [3/363]	1.6% (0.2%, 5.7%) [2/125]
Sensitivity analysis [†]	1.1% (0.3%, 2.8%) [4/363]	2.4% (0.5%, 6.9%) [3/125]
Proportion of adrenal metastasis from colon cancer	0.3% (0.0%, 1.5%) [1/363]	0% (0.0%, 2.9%) [0/125]
Proportion of patients who underwent additional adrenal examination [‡]	6.1% (3.8%, 9.0%) [22/363]	10.4% (5.7%, 17.1%) [13/125]
Percutaneous or excisional biopsy	15	11
Percutaneous	1	1
Excisional	14	10
Imaging test	18	10
Non-contrast CT	7	1
Contrast-enhanced CT	7	6
Magnetic resonance imaging	4	3

Data are proportions (95% CI) or number of patients. *Unless otherwise specified, patients with incomplete reference standard were regarded as not having malignant nodules. [†] By assuming that the proportion of patients having malignant adrenal nodules in the patients with incomplete reference standard (11 patients in the primary analysis, and 4 patients in the secondary analysis) was five percentage points higher than that of patients with complete reference standard. [‡] Patients could belong to multiple categories. *CI*, confidence interval; *CT*, computed tomography

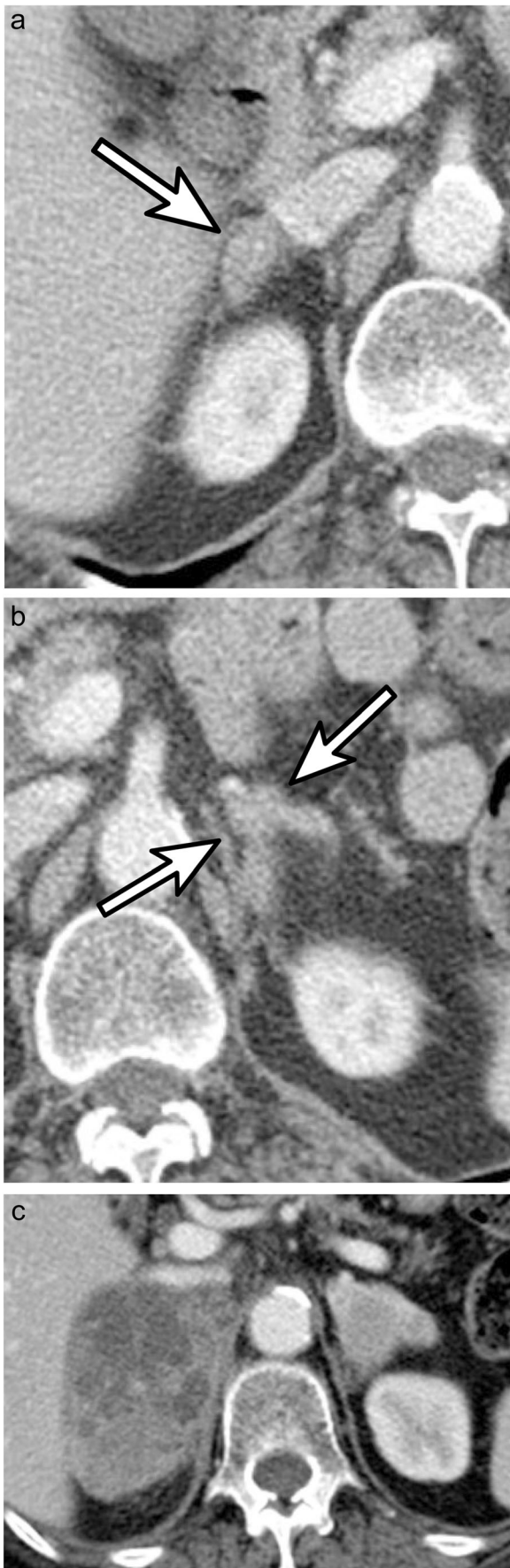


Fig. 2 A 78-year-old woman with ascending colon cancer and malignant adrenal nodules. Contrast-enhanced transverse image of staging CT shows (a) a 15-mm nodule (arrow) in the right adrenal gland, and (b) a 12-mm nodule (arrow) in the left adrenal gland. These two nodules and another small nodule in the left gland (not seen in the image) were detected via retrospective CT image review but were omitted from the official CT report. Liver MRI and chest CT performed at the time of staging did not show any sign of other distant metastasis. The patient received right hemicolectomy for the cancer, which was confirmed as pT2N0 stage. (c) Contrast-enhanced transverse image of follow-up CT 6 months after surgery shows bilateral adrenal masses, without any evidence of other metastasis on CT. These nodules were adjudicated as metastases from the ascending colon cancer

of patients with pathologically confirmed colorectal cancer or those who ended up receiving pathologic confirmation of their adrenal nodules. By carefully identifying even those with metastases that were considered resectable in multidisciplinary conferences at the time of staging, we tried to make our patient sample relevant to the clinical question in hand.

Our study had limitations. First, this retrospective study took place in a single center. Further studies are needed by including a larger number of patients from other regions with differing cancer epidemiology. Second, pathologic confirmation was obtained in only a portion of the patients with adrenal nodules. However, it is very unlikely that any malignant nodule was missed at our final adjudication, considering the long follow-up duration (median, 49 months). Third, although subgroup analysis would be extremely beneficial for refining the indications for selective use of additional imaging, we unfortunately could not perform the pre-planned subgroup analysis due to



Fig. 3 A 67-year-old man with sigmoid colon cancer and a malignant nodule. Contrast-enhanced transverse CT image shows a 74-mm nodule (arrow) in the left adrenal gland. The nodule was confirmed as adrenocortical carcinoma after adrenalectomy. The colon cancer was confirmed as pT1 stage after polypectomy

low event rates. Lastly, further studies would be needed to weigh the cost against the diagnostic yield of additional tests for characterizing CT-detected adrenal nodules.

While detection of an adrenal nodule is common on staging CTs of patients with otherwise resectable colorectal cancer, these nodules are rarely malignant. Current guidelines need revision toward more selective use of additional imaging for such adrenal nodules.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00330-022-08892-3>.

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Declarations

Guarantor The scientific guarantor of this publication is Yoon Jin Lee.

Conflict of interest The authors of this manuscript declare relationships with the following companies: Yoon Jin Lee and Hae Young Kim received research grants from Seoul National University Bundang Hospital. Other authors declare there is no conflict of interest.

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Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology

- retrospective
- observational
- performed at one institution

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