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CHEST

Thoracic recurrence in patients with curatively-resected colorectal cancer: incidence, risk factors, and value of chest CT as a postoperative surveillance tool

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Abstract

Objective To investigate the incidence of thoracic recurrence and the diagnostic value of chest CT for postoperative surveillance in curatively-resected colorectal cancer (CRC) patients.

Methods This retrospective study consisted of 648 CRC patients (M:F, 393:255; mean age, 66.2 years) treated with curative surgery between January 2010 and December 2012. The presence of CRC recurrence over follow-ups was analysed and recurrence-free survival and risk factors of recurrence were assessed using Kaplan–Meier analysis with log-rank test and Cox-regression analysis, respectively.

Results Over a median follow-up of 57 months, thoracic recurrence occurred in 8.0% (52/648) of patients with a median recurrence-free survival rate of 19.5 months. Among the 52 patients with thoracic recurrence, 18 (2.7%) had isolated thoracic recurrence, and only five (0.8%) were diagnosed through chest CT. Risk factors of overall thoracic recurrence included age, positive resection margin, presence of venous invasion, positive pathologic N-class, and presence of abdominal recurrence (odds ratio [OR] = 1.78, 19.691, 2.993, 2.502, and 31.137; $p = 0.045$, 0.004, 0.001, 0.005, and $p < 0.001$, respectively). As for isolated thoracic recurrence, serum carcinoembryonic antigen level ≥ 5 ng/mL during postoperative follow-up (OR = 9.112; $p < 0.001$) was demonstrated to be the only predictive factor. There were no thoracic recurrences in patients with CRC stages 0 and I.

Conclusion In patients with curatively-resected CRCs, routine surveillance using chest CT may be of limited value, particularly in those with CRC stages 0 or I, as recurrence only detectable through chest CT was shown to be rare.

Key Points

- *Postoperative thoracic recurrence only detectable through chest CT was shown to be rare.*
- *There were no thoracic recurrences in colorectal cancers stage 0 and I.*
- *Postoperative surveillance chest CT is of limited value in patients with curatively resected colorectal cancers.*

Keywords Colorectal cancer · Thorax · Recurrence · Follow-up studies · Tomography, x-ray computed

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Abbreviations

CEA Carcinoembryonic antigen
CRC Colorectal cancer

Introduction

Colorectal cancer (CRC) is the 3rd most common cancer and the 4th leading cause of cancer death worldwide [1]. It would appear fortunate that approximately 80% of newly diagnosed CRCs present without metastases at diagnosis, and, therefore,

are eligible for curative surgical treatment. However, despite curative surgical treatment and adjuvant chemotherapy, 30–50% of these patients experience recurrence over their follow-ups [2–6], 90% of which occurs within 5 years after surgery, with most occurring in the first 2 years [7–10].

Chest CT has become accepted as a key postoperative surveillance tool for curatively resected CRC patients in many professional guidelines [11–15] as the lung is the 2nd most common organ of metastases from CRC following liver, constituting approximately 10–20% of all metastases, and is usually accompanied by metastases in other parts of the body [11, 16, 17]. Long-term (5-year) survival rates in CRC patients with pulmonary recurrence and subsequent metastasectomy has been reported to range between 37 to 56.2%, and thus there has been a general acceptance of aggressive pulmonary metastasectomy in appropriately selected CRC patients [18–24].

However, considering the low incidence of thoracic recurrence, routine chest CT without any specific indication may be of limited value and may actually pose a great burden to the patient, leading to unnecessary cost, radiation exposure, or even erroneous recall for false positive CT findings [11, 16, 17]. In addition, abdominal imaging studies such as abdominal CT which are routinely acquired for postoperative surveillance can actually cover the lower part of the thorax, which would obviate the need for routine chest CTs. To our knowledge, however, there have been no studies examining the necessity of routine chest CTs as part of the postoperative surveillance protocol in CRC patients nor for the risk factors of isolated thoracic recurrence in this patient population. Therefore, the purpose of this study was to investigate the incidence of overall and isolated thoracic recurrence and the diagnostic value of chest CT for postoperative surveillance in patients with curatively resected CRCs.

Materials and methods

This retrospective study was approved by the Institutional Review Board of Seoul National University Hospital with waiver of the requirement for patients' informed consent.

Study cohort and data collection

One author (J.H.L., with 6 years of experience in thoracic and abdominal radiology) searched the surgical and pathologic records of our hospital between January 2010 to December 2012 and identified a total of 1479 patients who had undergone curative colorectal surgery without neoadjuvant treatment. Two radiologists (J.H.L. and C.M.P., with 19 years of experience in thoracic radiology) then reviewed all of the available radiologic, pathologic, and clinical records of these 1479 patients. Patients whose clinical and radiologic data met all of the following criteria were included in the study population: patients (a) whose pathology was proven as primary CRC, (b) with at least one available postoperative surveillance chest CT and abdominal CT or MRI, (c) without other known malignancies, and (d) without metastases at initial presentation. Finally, a total of 648 patients (393 men and 255 women; mean age, 66.17 ± 10.85 years; range 30–95 years) with CRC comprised our study population (Fig. 1).

Clinical and radiological evaluation for follow-up of the study cohort

The follow-up strategy of our hospital for CRC patients who had undergone curative CRC surgeries is as follows: abdominal CT, serum carcinoembryonic antigen (CEA) level exam,

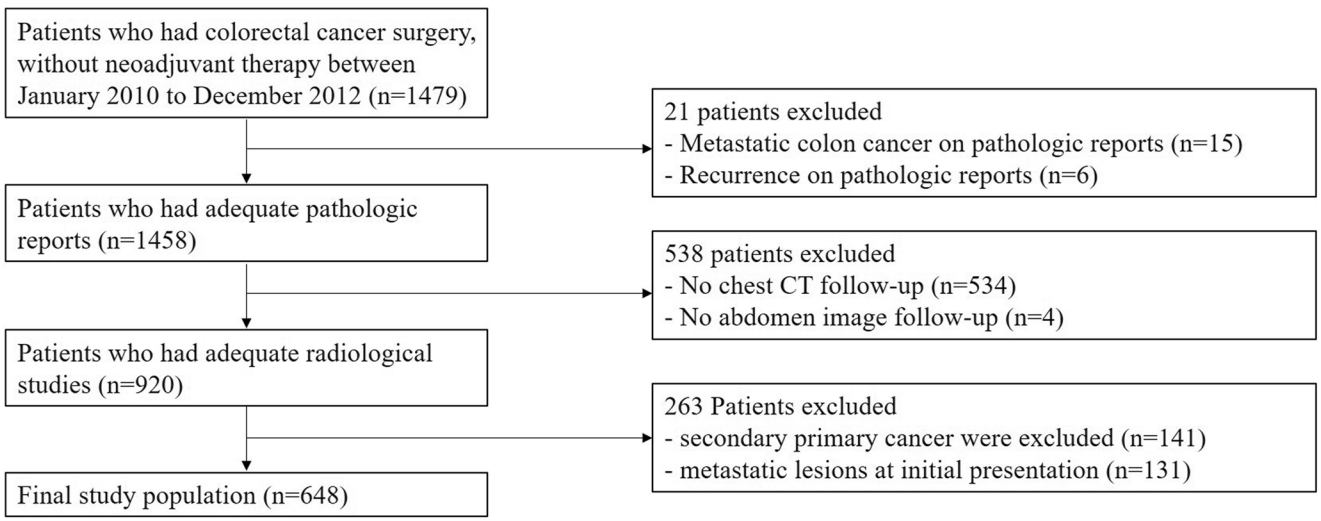


Fig. 1 Flowchart showing the study cohort selection process

chest x-ray every six months, and chest CT annually. In certain clinical situations (e.g., the patient's clinical condition), additional image-related decisions were made on a case-by-case basis. With regard to the anatomic coverage of each imaging study, chest CT covered the areas from the lung apex to the costophrenic recess, and abdominal imaging studies such as abdominal CT covered anatomical structures from the dome of the right diaphragm to the pelvis.

We searched the electronic medical records including all of the available clinical and demographic characteristics of all 648 patients included in this study and reviewed the pathologic reports of their CRCs. Serum CEA values at their last follow-up in patients without recurrence and those at initial detection in patients with thoracic metastases, if any, were recorded. Of the pathological reports, poor differentiation, positive surgical margin, and angiolymphatic, venous, or perineural invasion were designated as high-risk features for recurrence [13]. For reference, their pathological stage was recorded according to the 8th edition of the American Joint Cancer Committee (AJCC) tumour, node and metastasis (TNM) cancer staging system [25].

In this study, 'isolated thoracic recurrence' was designated as the following cases: (a) the thorax was the only recurrence site over follow-ups or (b) the thorax was the initial recurrence site when recurrences occurred in two or more body parts including the thorax over follow-ups. The reference standard for CRC recurrence was the patients' clinical, radiological, and pathologic information, as pathological confirmation was not always possible for every suspicious lesion in real clinical practice. At first, one author (E.J.H., with 8 years of experience in thoracic and abdominal radiology) initially checked all of the available medical records, radiological reports, and follow-up imaging studies in order to detect CRC recurrence. Thereafter, all indeterminate cases at initial evaluation were resolved through a consensus discussion between three radiologists (E.J.H., C.M.P., and I. J. with 12 years of experience in abdominal radiology). For the evaluation of CRC recurrence, the radiologists reviewed the radiological studies by comparing them with other imaging examinations or follow-up studies, and clinical information. In this evaluation step, anatomical locations of the thoracic recurrences, e.g., lung parenchyma or pleura, if any, were recorded. In addition, we assessed whether the thoracic recurrence was covered by abdominal CT as the clinical relevance of chest CT during postoperative surveillance was one of the main purposes of this study.

During the radiological evaluation, 2938 CT examinations of the chest, 5805 CT examinations of the abdomen with the pelvis, 130 MR examinations of the abdomen, and 122 PET-CT examinations were assessed. A total of 10 lesions in 10 patients (8 lung parenchymal lesions, 1 liver lesion, 1 peritoneal lesion) were not initially able to be determined as recurrence. However, after consensus reading by three radiologists, two lesions were determined to be recurrences (one lung recurrence which grew on follow-up chest CT and one peritoneal recurrence which was progressively prominent and combined with abdominal wall metastasis on follow-up abdomen CT); the other eight lesions were determined not to be metastases, e.g., polygonal-shaped lung parenchymal lesions or increased peripheral eosinophilic count in the case of liver lesions.

As an alternative to chest CT in detecting isolated thoracic recurrences which were not detected with abdominal CT, chest radiographs taken at the same time as chest CT were reviewed and investigated.

All imaging studies were reviewed on the picture archiving and communication system (PACS Viewer, Infinitt Healthcare, Seoul, Korea).

Statistical analysis

In this study, we assessed the incidence of isolated and overall thoracic recurrence and ascertained predictive factors including primary and secondary end points. For the evaluation of isolated thoracic recurrence, 76 patients with abdominal recurrences as their first recurrence were not eligible and thus were excluded.

All patients were categorised into two groups according to whether or not they had thoracic recurrence over follow-ups. Kaplan–Meier analyses with the log-rank test were used to analyse the clinical, pathological, and radiological variables in the two groups. Variables including age, sex, pathological type, pathological differentiation, tumour location, tumour size, surgical margin, angiolymphatic, venous, perineural invasion, and T-class and N-class of each CRC were designated as 'risk factors of disease recurrence' as these factors were revealed at the time of surgical resection. CEA values on follow-ups, recurrence in the abdomen, and the interval between surgery and abdominal recurrence (abdominal recurrence-free interval) were referred to as 'signs of recurrence during surveillance' during the follow-up period. For CEA values on follow-ups, the cut-off value was set at 5 ng/ml [19, 26]. Thoracic recurrence-free interval and abdominal recurrence-free interval were defined as the interval from the curative operation of CRC to the occurrence of thoracic or abdominal recurrence. These two types of variables, 'risk factors' and 'sign of recurrence', were analysed separately as the two kinds of information were obtained at different time points. Subsequently, multivariate Cox proportional hazard regression analyses were performed to evaluate the risk factors of thoracic recurrence, with all variables used as input variables. Backward elimination mode was employed with iterative entry of variables based on the results (p value < 0.05) and removal of variables based on likelihood ratio statistics with a probability of 0.05.

A p value < 0.05 was considered to indicate a statistically significant difference, with all statistical analyses performed using SPSS ver. 20.0 (SPSS Inc., Chicago, IL, USA) and Medcalc ver. 12.0 (Medcalc Software, Mariakerke, Belgium).

Results

Baseline clinical and pathological features and profile of recurrence on follow-up

Demographic features of the 648 patients and pathologic characteristics of their CRCs are summarised in Table 1. Of the 573 stage II and III CRCs, 367 had at least one high-risk feature (poor differentiation, n = 27; positive surgical margin, n = 2; angiolymphatic invasion, n = 181; venous invasion, n = 60; perineural invasion, n = 147), and the mean CEA level at the last follow-up or at the detection of thoracic metastases was 6.90 ± 48.16 ng/ml (range, 0.0–1022.6 ng/ml).

During the follow-up periods of all 648 patients (median follow-up duration, 57.0 months; interquartile range [IQR], 50–62 months; range, 2–87 months), 102 out of 648 patients (15.7%) had recurrence (Fig. 2), with thoracic and abdominal recurrences developing in 52 (8.0%) and 91 patients (14.0%), respectively. Median thoracic and abdominal recurrence-free intervals were 19.5 months (IQR, 12–36.25 months; range, 1–63.0 months) and 12.0 months (IQR, 4–29 months; range, 1–72 months), respectively (Table 2). Eighteen of the 52 thoracic recurrences and 44 of 91 abdominal recurrences were confirmed pathologically while the remaining recurrences were clinically diagnosed based on radiological evaluation and the physicians' decisions.

Among the 52 patients with thoracic recurrence, 18 (2.8% of all CRC patients) had isolated thoracic recurrence (median time to metastases detection, 18.5 months; range, 1–59 months) and

Table 1 Demographic and pathologic characteristics of 648 patients with colorectal cancer

Age (years)	66.17 ± 10.85	T-class	
Sex		Tis	3 (0.5%)
Male	393 (60.6%)	T1	38 (5.9%)
Female	255 (39.4%)	T2	77 (11.9%)
Adjuvant chemotherapy		T3	449 (69.3%)
Yes	534 (82.4%)	T4a	67 (10.3%)
No	114 (17.6%)	T4b	14 (2.2%)
Pathological type		N-class	
Classical adenocarcinoma	611 (94.3%)	N0	315 (48.6%)
Non-classic type[a]	37 (5.7%)	N1a	121 (18.7%)
Differentiation		N1b	87 (13.4%)
Well differentiated	88 (13.6%)	N1c	32 (4.9%)
Moderately differentiated	530 (81.8%)	N2a	62 (9.6%)
Poorly differentiated	30 (4.6%)	N2b	31 (4.8%)
Location		Stage	
Cecum	24 (3.7%)	0	3 (0.5%)
Ascending colon	143 (22.1%)	I	72 (11.1%)
Hepatic flexure	20 (3.1%)	IIA	210 (32.4%)
Transverse colon	45 (6.9%)	IIB	18 (2.8%)
Splenic flexure	9 (1.4%)	IIC	12 (1.9%)
Descending colon	40 (6.2%)	IIIA	33 (5.1%)
Sigmoid colon	320 (49.4%)	IIIB	258 (39.8%)
Rectosigmoid colon	34 (5.2%)	IIIC	42 (6.5%)
Rectum	13 (2.0%)		
		Stage II	240
Size (maximal diameter; cm)	4.74 ± 2.32 (range, 0.2 – 14.5)	Stage II with high risk[b]	84 (35.0%)
		Stage II without high risk[b]	156 (65.0%)

[a] Non-classic type: mucinous adenocarcinoma, signet ring cell carcinoma, serrated adenocarcinoma, medullary carcinoma, cribriform adenocarcinoma, mixed adenoneuroendocrine tumour

[b] High risk: poorly differentiated; Positive, close, or unknown surgical margin; angiolymphatic invasion; venous invasion; perineural invasion

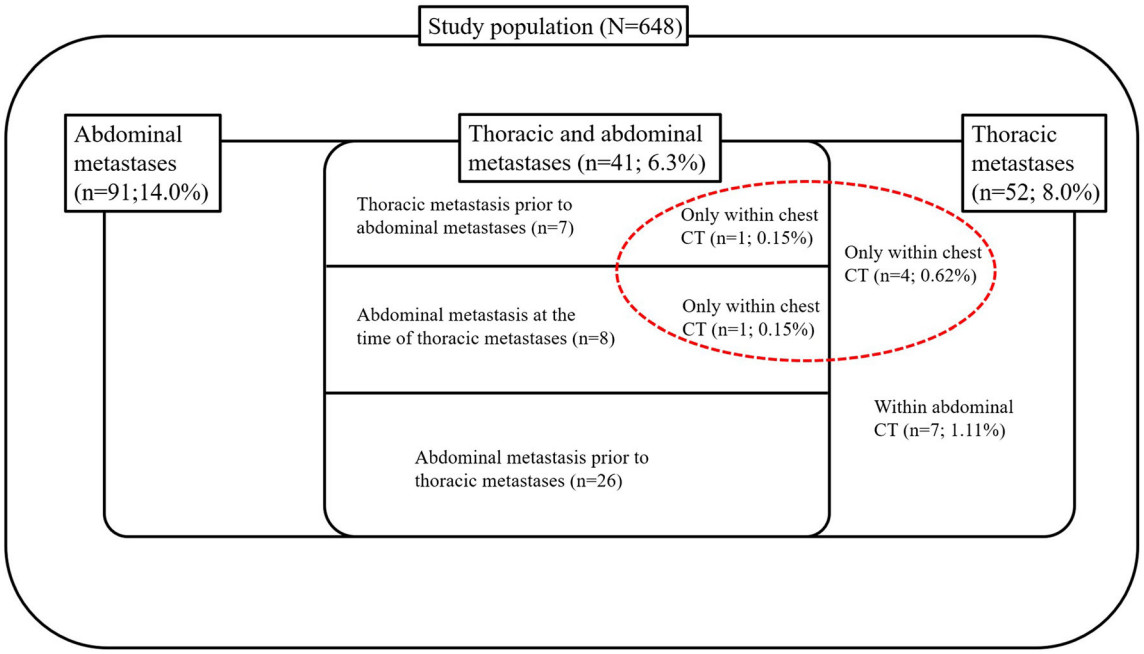


Fig. 2 Diagram showing the recurrence profile of curatively resected colorectal cancers without initial metastases. Only 5 of the 648 patients, approximately 0.8%, demonstrated the clinical relevance of routine postoperative chest CT in detecting thoracic recurrence beyond the coverage of abdominal CT

they were all CRC stage II (n = 6) or stage III (n = 12). Thirteen of these 18 cases were located in the lower lung and were covered by abdominal CTs. Of the 13 patients with isolated thoracic recurrence in the lower lung, all recurrent lesions were detected by abdominal CT in seven (Fig. 3), and some but not all recurrent lesions were detected on abdominal CT in the other six patients. In the remaining five patients (0.8%), all recurrent lesions were located beyond the range of abdominal CT, but were detectable on chest CTs (Fig. 4). Among these five patients, however, thoracic recurrences were demonstrated on chest radiographs in three patients, and only two of them were unable to be diagnosed as recurrence without chest CTs. These five patients and the characteristics of their primary CRCs are summarised in Table 3.

In this study, 89 patients had undergone PET-CT examinations, 20 of whom had PET-CT examinations taken at the time of diagnosis of thoracic recurrences. Interestingly, 18 out of these 20 patients showed hypermetabolism for the thoracic recurrences, while two located in the lung parenchyma (size, 0.6 and 0.5 cm) demonstrated no hypermetabolism on PET-CT. As for isolated thoracic recurrence, eight patients had available PET-CT examinations, seven of whom demonstrated hypermetabolic lesions, while one patient did not have any hypermetabolic lesion on PET-CT.

Risk factors and signs of thoracic recurrence

In the analysis of overall thoracic recurrence, age (OR = 1.780; 95% confidence interval [CI], 1.012–3.131; p = 0.045), positive surgical margin (OR = 19.691; 95% CI, 2.541–152.607; p = 0.004), venous invasion (OR=2.993; 95% CI, 1.583–5.658; p = 0.001), and positive N-class (OR = 2.502; 95% CI, 1.316–4.759; p = 0.005) were shown to be significant risk factors of thoracic recurrence. Presence of abdominal recurrence (OR = 13.137; 95% CI, 15.968-60.714; $p < 0.001$) was also demonstrated to be a significant warning sign of thoracic recurrence (Table 4).

As for isolated thoracic recurrence (n = 18), serum CEA ≥ 5 ng/ml (OR = 9.112; 95% CI, 2.634–31.527; $p < 0.001$) was demonstrated to be a significant warning sign of recurrence during surveillance (Table 5).

The incidence of thoracic recurrences according to the pathological stage of CRCs is as follows: no thoracic recurrence in CRC stages 0 or I (n = 75); 13 cases (5.4%; 13/240) in stage II (n = 240); and 39 cases (11.7%; 39/333) in stage III (n = 333).

Discussion

Recent studies [18–23] have reported that the aggressive resection of pulmonary metastases from CRC can improve patients' prognosis, resulting in 5-year survival rates of 37% to as high as 56.2%. In addition, as the size, number, and laterality of pulmonary metastases are known to be prognostic factors associated with the survival of CRC patients after metastasectomy [19, 22–24], the early detection of lung metastases prior to a size increase or their dissemination has been thought to be clinically critical for a better prognosis. Thus, in

Table 2 Profile of cases with identified recurrence from colorectal cancer

Abdominal metastasis	91
Pathologic confirmation for abdominal metastasis	44
Abdominal recurrence-free interval	12.0 months (IQR, 4–29 months; range, 1–72 months)
Initial abdomen metastasis site	
Liver	42 (46.2%)
Lymph node	21 (23.1%)
Peritoneum	19 (20.9%)
Local recurrence	15 (16.5%)
Bone (spine)	3 (3.3%)
Abdominal wall	3 (3.3%)
Adrenal gland	1 (1.1%)
Duodenum	1 (1.1%)
Inguinal area	1 (1.1%)
Mesentery	1 (1.1%)
Kidney	1 (1.1%)
Biliary duct	1 (1.1%)
Bladder	1 (1.1%)
Vagina	1 (1.1%)
Thorax metastasis	52
Pathologic confirmation for thoracic metastasis	18
Thoracic recurrence-free interval	19.5 months (IQR, 12–36.25 months; range, 1–63.0 months)
Initial thorax metastasis site	
Lung parenchyma	48 (92.3%)
Lymph node	12 (23.1%)
Pleura	4 (7.7%)
Airway (trachea, bronchus)	2 (3.8%)
Recurrences in other body parts besides the thorax	42
Abdomen	37
Bone	1
Abdomen, bone	1
Abdomen, brain	2
Abdomen, bone, brain	1

IQR interquartile range

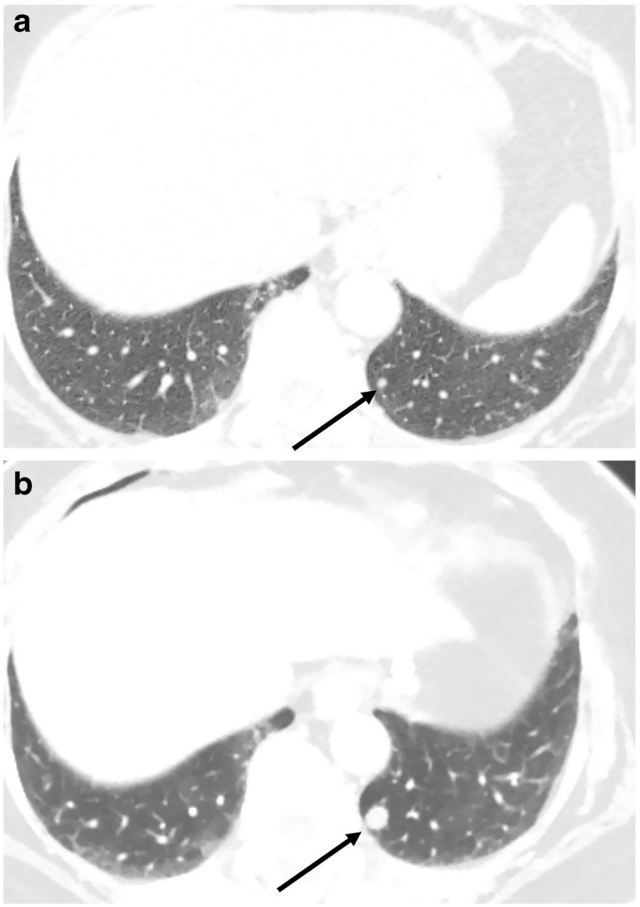
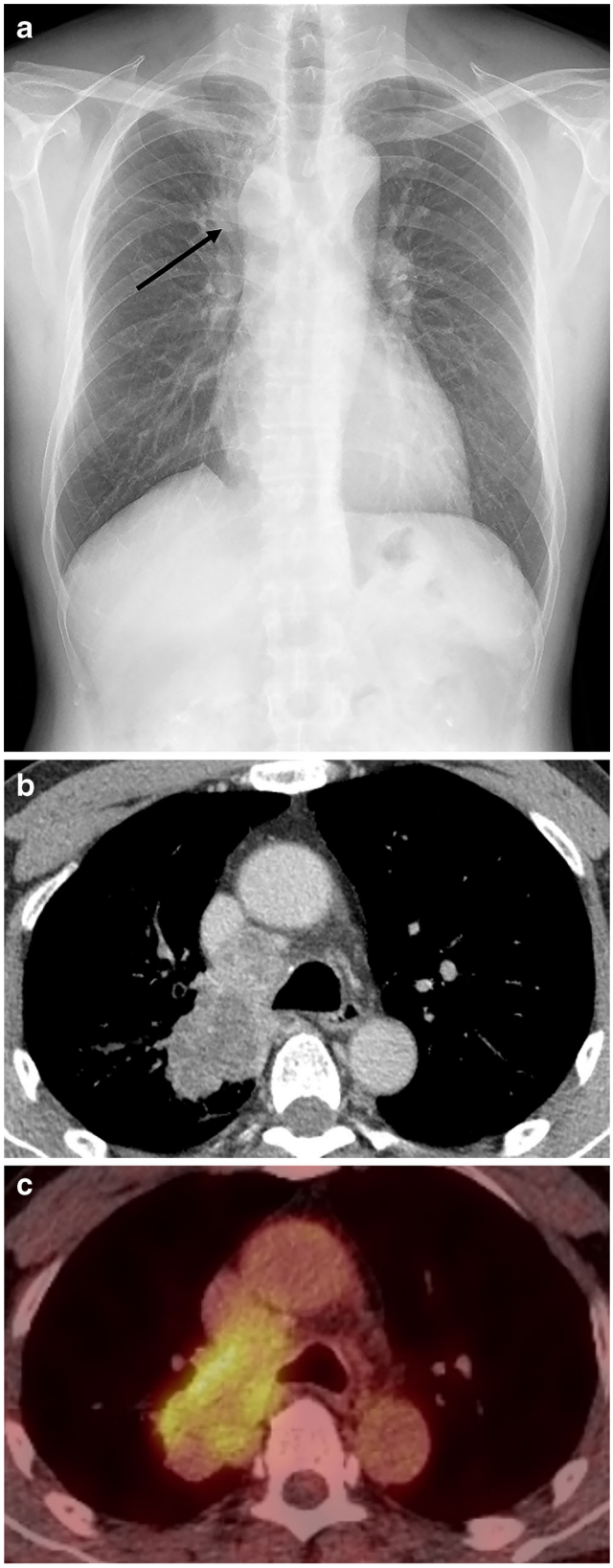


Fig. 3 A representative case of thoracic recurrence as initial recurrence fully covered by abdominal CT. A 59-year-old female who underwent cecal cancer operation for pathological stage 3B (T3, N2a, M0) cancer. **a** Without any abdominal metastasis, a less-than-5-mm-sized nodule in the left lower lobe was newly detected on both follow-up chest and abdominal CT taken 37 months after colorectal cancer operation (black arrow). **b** Six months later, the size of the lesion increased and the authors identified it as thoracic recurrence (black arrow). This nodule was pathologically confirmed to be metastatic adenocarcinoma by wedge resection. This lung recurrence was located in the left lower lobe which was sufficiently covered by abdominal CT

this context, it may appear reasonable for every CRC patient who undergoes curative surgical resection to also undergo postoperative surveillance chest CT on a regular basis. However, considering the very low incidence of thoracic recurrence shown in our study, particularly in patients with early-stage CRCs (stages 0 and I), routine surveillance chest CT may not be clinically appropriate for every patient, and may instead lead to unnecessary diagnostic examinations, unnecessary consumption of medical and financial resources, risk of complications, and additional radiation hazard, especially in younger patients. Therefore, we cautiously suggest that postoperative surveillance chest CT for thoracic recurrence should not be performed outside of specific indications and that abdominal CT may suffice in providing sufficient coverage in patients with curatively resected CRCs.

In this regard, knowledge of the overall and isolated thoracic recurrence rates as well as their predictive factors may help determine the most appropriate candidates for routine chest CT surveillance. In the present study, age, positive surgical margin, venous invasion, positive N-class of the primary CRCs, abdominal recurrence, and serum CEA ≥ 5 ng/ml were shown to be predictive factors of thoracic recurrence and potential indicators of chest CT during postoperative surveillance of CRCs. Specifically, patients with serum CEA ≥ 5 ng/ml during postoperative surveillance should undergo



◀ **Fig. 4** A representative case of initial recurrence in the thorax which was beyond the coverage of abdominal CT. **a** Chest radiograph taken 59 months after the operation demonstrated a bulging opacity at the right paratracheal area (black arrow). **b** On chest CT taken on the same day of the chest radiograph, an approximately 4.8-cm mass on the right upper lobe and lymph node enlargement at the right paratracheal area were detected without any metastasis in the abdomen and lower thoracic area. **c** Additionally, performed PET-CT revealed hyper-metabolism at the right upper lobe lesion and the right paratracheal lymph node. Cytology by bronchoscope confirmed these lesions as metastatic adenocarcinoma from the colon

chest CT even if they have no demonstrable recurrence in the abdomen. In addition, our study results showed that all 18 cases of isolated thoracic recurrence occurred in the first 5 years after CRC surgery, 14 of which (77.8%) occurred within the first 2 years similar to that reported in other previous studies [7–10]. Based on this result, postoperative surveillance for the thorax may be more effective in the early postoperative period than in their later periods.

Although thorax surveillance is a generally accepted strategy in the CRC postoperative period, there has not yet been a universally accepted guideline for the utilisation of surveillance chest CT in patients who underwent curative surgery for CRC [11–15]. At present, the National Comprehensive Cancer Network (NCCN) suggests chest CT every 6 to 12 months for up to 5 years in patients with stage II or III CRCs, and no radiological examination for CRCs of stage I [13]. Similarly, the American Society of Clinical Oncology (ASCO) recommends chest CT every 6 to 12 months for the first 3 years for CRCs of stage II or III; however, ASCO does not provide any specific guidelines for postoperative radiological surveillance in CRC stage I patients due to the minimal amount of available evidence in this population [12]. On the other hand, the European Society for Medical Oncology (ESMO) recommends thorax surveillance only for patients with higher risk of recurrence [11], while the National Institute of Health and Care Excellence (NICE) and the British Columbia Medical Association suggest regular thorax-surveillance with a minimum of two CTs of the chest in the first 3 years for all patients [14, 15]. To the contrary, chest CT is not included in the postoperative surveillance protocol issued by the New Zealand Group [27]. In our study, we found that there were no cases of thoracic recurrence in patients with CRCs of stage 0 or stage I, and that all CRCs with thoracic recurrences were of stage II or stage III, which supports the NCCN guideline of not recommending chest CT in patients with CRC stage I [13]. Therefore, according to our observation and that of previous studies, routine chest CT surveillance may be obviated in patients with CRCs of stage 0 and I.

Interestingly, we found that the incidence of isolated thoracic recurrence only detectable through chest CT was only 0.8% (5/648), and that in the majority of patients with isolated thoracic recurrence (72.2%; 13/18), thoracic recurrences were detectable on abdominal CT even though abdominal CT was not able to demonstrate every thoracic recurrence. Additionally, it is interesting that four of these five isolated thoracic

Table 3 Profiles of patients whose thoracic recurrence were demonstrable only on chest CT

Patient number	1	2	3	4	5
Sex	Male	Male	Female	Male	Male
Age (years)	63	81	61	69	68
Pathologic type	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
Differentiation	Moderate	Moderate	Moderate	Moderate	Well
Tumour Location	Sigmoid colon	Transverse colon	Sigmoid colon	Sigmoid colon	Sigmoid colon
Maximal size of original colorectal cancer (cm)	4.5	6.0	5.0	2.2	1.3
T stage	3	3	4a	2	2
N class	2a	Negative	1a	2a	1a
Stage	IIIB	IIA	IIIB	IIIB	IIIA
Thoracic recurrence-free interval (months)	59	54	17	23	6
Initial location of thoracic recurrence	Lung (right upper lobe), pleura, lymph node, trachea	Lung (right lower lobe	Lung (right upper lobe)	Lung (right upper lobe)	Lung (left upper lobe)
CEA level (ng/ml)	6.6	3.0	0.9	2.4	1.7
Demonstrable thoracic metastasis on chest x-ray	Yes	No	Yes	Yes	No
High risk feature	None	None	None	Angiolymphatic invasion	None
Abdominal recurrence	None	None	None	None	Yes (45 months after thoracic recurrence)

CEA carcinoembryonic antigen

recurrences which were only detectable through chest CT were diagnosed as stage III CRCs and that three lung recurrences of these five cases were also demonstrated on plain chest radiographs taken around the same time of chest CT. Thus, plain chest radiographs may also be a possible alternative surveillance modality, particularly in patients with a low risk for recurrence. Further prospective studies with a large study population are warranted to confirm our observation.

Finally, according to several guidelines [11–13], PET-CT is not recommended at present for the postoperative surveillance of curatively resected CRCs. And PET-CT has a limitation in detecting small metastases, especially those smaller than 1 cm [28]. Nevertheless, we believe that PET-CT may have potential as a postoperative surveillance tool in patients with suspected recurrence of CRC based on clinical suspicions or elevated CEA levels as PET-CT can be sensitive for the detection of CRC recurrence [29, 30]. Indeed, in our study, we found that thoracic recurrences appeared as hypermetabolic lesions on PET-CT in most of the patients (18 out of 20) who had thoracic recurrences and had undergone PET-CT exams in this study. Further studies are also warranted to determine the role of PET-CT in patients with curatively resected CRCs.

There are several limitations that we would like to mention. First, this study was of a retrospective nature and, therefore, radiological examinations and patients' management strategies were not uniformly performed. Second, as the study did not cover follow-up periods of more than 5 years, there may have been the possibility of missing late recurrences. However, we found that most thoracic recurrences occurred within the first 2 years of CRC surgery and thus our follow-up periods may have been sufficient in this regard. Third, although the study population is not small, the number of thoracic recurrences was relatively small, posing a potential issue in statistical power. For example, although CEA levels ≥ 5 ng/ml were statistically proven to be a sign of potential recurrence, this condition was actually met in only 3 out of 18 isolated thoracic recurrences and thus may have limited clinical value in detecting recurrence. Fourth, KRAS mutation status of CRCs was not evaluated in this study as the test was not performed at our institution during the study period. KRAS mutant CRCs have been reported to have lung and brain metastases more frequently than its wild-type counterparts [31], and increasing evidence has mounted for the negative prognostic role of KRAS mutations in CRCs [31, 32]. Thus, further studies dealing with the utility of postoperative surveillance examinations including chest CT according to the presence of KRAS mutation is warranted. Finally, there may have been variability in how much of the lung bases were covered on abdominal CT across different hospitals and

Table 4 Predictive factors of overall thorax recurrence in patients with colorectal cancer (univariate Kaplan-Meier analyses with the log-rank test and multivariate Cox proportional hazard regression analyses with backward elimination mode were used)

Risk factors for disease recurrence		Univariate analysis					Multivariate analysis		
		No. of patients (N = 648)	No. of thoracic recurrence (N = 52)	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Age	< 67 years	322	21	1.628	0.945, 2.805	0.081	1.780	1.012, 3.131	0.045
	≥ 67 years	326	31						
Sex	Female	255	20	1.063	0.610, 1.852	0.830			
	Male	393	32						
Pathologic type	Classical adenocarcinoma	611	49	0.957	0.305, 3.003	0.941			
	Non-classical type[a]	37	3						
Differentiation	Well and moderately differentiated	618	50	0.853	0.229, 3.174	0.825			
	Poorly differentiated	30	2						
Location	From cecum to sigmoid	281	25	0.774	0.446, 1.344	0.355			
	Rectosigmoid junction and rectum	367	27						
Size	< 2cm	59	1	6.085	2.522, 14.681	0.041			
	≥ 2cm	589	51						
Surgical margin	Free	646	51	9.345	0.244, 3573.128	0.007	19.691	2.541, 152.607	0.004
	Involved by cancer	2	1						
Angiolymphatic invasion	Absent	454	32	1.550	0.850, 2.826	0.121			
	Present	194	20						
Venous invasion	Absent	586	39	3.568	1.349, 9.434	< 0.001	2.993	1.583, 5.658	0.001
	Present	62	13						
Perineural invasion	Absent	501	33	1.933	1.013, 3.688	0.020			
	Present	147	19						
T-class	Tis, 1, 2	118	3	4.178	2.127, 8.205	0.009	3.090	0.957, 9.979	0.059
	T3, 4	530	49						
N-class	N0	315	13	2.826	1.641, 4.868	0.001	2.502	1.316, 4.759	0.005
	N1, 2	333	39						
Signs of recurrence during surveillance									
CEA level (ng/ml)[b]	< 5	603	34	9.904	2.871, 34.172	< 0.001			
	≥ 5	45	18						
Abdomen recurrence-free interval	> 24 months	553	23	13.284	5.056, 34.901	< 0.001			
	≤ 24 months	95	29						
Abdomen metastasis	Absent	557	11	30.280		< 0.001	31.137	15.968, 60.714	< 0.001
	Present	91	41						

N number, *HR* hazard ratio, *CI* confidence interval, *CEA* carcinoembryonic antigen

[a] Non-classic type: mucinous adenocarcinoma, signet ring cell carcinoma, serrated adenocarcinoma, medullary carcinoma, cribriform adenocarcinoma, mixed adenoneuroendocrine tumour

[b] Serum CEA levels at their last follow-up or at initial detection of thoracic metastasis, if any, were recorded

Table 5 Predictive factors of isolated thorax recurrence in patients with colorectal cancer (univariate Kaplan-Meier analyses with the log-rank test and multivariate Cox proportional hazard regression analyses with backward elimination mode were used)

Risk factors for disease recurrence		Univariate analysis					Multivariate analysis		
		No. of patients (N = 564)	No. of isolated thoracic recurrence (N = 18)	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Age	< 67 years	294	8	1.482	0.586, 3.746	0.404			
	≥ 67 years	270	10						
Sex	Female	220	7	1.049	0.408, 2.692	0.922			
	Male	344	11						
Pathologic type	Classical adenocarcinoma	533	18			0.283			
	Non-classical type[a]	31	0						
Differentiation	Well and moderately differentiated	540	18			0.359			
	Poorly differentiated	24	0						
Location	From cecum to sigmoid	238	8	0.879	0.344, 2.247	0.786			
	Rectosigmoid junction and rectum	326	10						
Size	< 2cm	59	1	2.249	0.534, 9.476	0.418			
	≥ 2cm	505	17						
Surgical margin	Free	563	18			0.851			
	Involved by cancer	1	0						
Angiolymphatic invasion	Absent	405	14	0.743	0.265, 2.083	0.598			
	Present	159	4						
Venous invasion	Absent	521	16	1.589	0.239, 9.391	0.533			
	Present	43	2						
Perineural invasion	Absent	452	15	0.793	0.251, 2.509	0.713			
	Present	112	3						
T-class	Tis, 1, 2	116	2	2.289	0.754, 6.951	0.256			
	T3, 4	448	16						
N-class	N0	289	6	2.067	0.820, 5.208	0.138	2.067	0.776, 5.509	0.146
	N1, 2	275	12						
Signs of recurrence during surveillance									
CEA level (ng/ml)[b]	< 5	550	15	9.088	0.377, 219.116	< 0.001	9.112	2.634, 31.527	< 0.001
	≥ 5	14	3						

N number, *HR* hazard ratio, *CI* confidence interval, *CEA* carcinoembryonic antigen

[a] Non-classic type: mucinous adenocarcinoma, signet ring cell carcinoma, serrated adenocarcinoma, medullary carcinoma, cribriform adenocarcinoma, mixed adenoneuroendocrine tumour

[b] Serum CEA levels at their last follow-up or at initial detection of thoracic metastasis, if any, were recorded

regions. For coverage of the whole liver using abdominal CT, we believe that bilateral lung bases at the level of the diaphragm should certainly be scanned at abdominal CT.

In conclusion, isolated thoracic recurrence, particularly those only detectable through chest CT was shown to be rare in patients with curatively resected CRC, and thus routine postoperative surveillance with chest CT may be of limited value, particularly in those with CRC stage 0 or I.

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Compliance with ethical standards

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Ethical approval Institutional review board approval was obtained.

Methodology
- retrospective
- observational study
- performed at one institution

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