Role of Ultrasonography in the Surveillance of Disease-Free Patients with Colorectal Cancer: a Retrospective Audit

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Abstract

Close surveillance of colorectal cancer (CRC) patients is helpful as early detection of resectable metastasis has a survival benefit. Ultrasonography (USG) is a frequently used modality to detect liver recurrence, although international guidelines do not include it. To evaluate the potential added role of USG in early detection of CRC recurrence. We performed a retrospective analysis of 230 patients of colorectal cancer treated at our institute in 2013–2014 who underwent abdominal USG for surveillance. 77/230 (33%) developed recurrence, with liver being the second most common site (22/230). 5/230 (2%) patients had recurrent disease first detected on USG, four of which also had raised serum CEA (carcinoembryonic antigen) levels. There were three false positive and four false-negative cases on USG. There was no added advantage of USG for early detection of CRC recurrence.

Keywords Colorectal cancer · Surveillance · Ultrasonography

Introduction

Colorectal cancer (CRC) is one of the five most commonly diagnosed cancers and causes of cancer death worldwide [1]. Surgical resection is the primary treatment modality for patients with localized colorectal cancer. However, about 30–40% of these patients develop recurrence, most of which occur within 2 years of surgery [2–6]. Unlike most other cancers, surgical resection of metastatic disease (as for example resectable hepatic metastases), if feasible, offers survival advantage [2, 7–9]. Hence, it is important to keep these patients under surveillance to catch recurrence early.

Although patients who are treated with curative intent are put on surveillance, there is no universally accepted surveillance protocol. The guidelines and practices across various countries and regions differ and are influenced by local health

care policies and resource availability. Clinical examination, evaluation of carcinoembryonic antigen (CEA), colonoscopy, and imaging are amongst the tests for most of the suggested follow-up regimens across the globe. Some of the common international guidelines on surveillance are listed in Table 1 [3, 10–14].

It must be noted that almost all guidelines recommend annual CT follow-up, with USG surveillance not recommended by any society. However, oncologists often feel more comfortable having more frequent imaging follow-up with either an abdominal ultrasound or a CT depending on the various clinical factors and patient affordability. The rationale for this practice is early detection of liver metastasis, which is one of the most common sites of recurrence in CRC. The ready availability and relative affordability of USG makes this a feasible option for most. The aim of our study was to evaluate whether ultrasonography of the abdomen has any added advantage in early detection of abdominal recurrence, particularly in the liver.

Materials and Methods

We performed a post-hoc analysis on an IRB-approved prospective study on colorectal cancer done in our institute in 2013–2014 [15]. We retrospectively reviewed the radiology

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Table 1 International guidelines on surveillance protocols for colorectal cancer [3, 10–14]

Society	Clinical examination	CEA	Colonoscopy	Imaging
NCCN	Every 3–6 months for 2 years, then every 6 months for 3 years	Every 3–6 months for 2 years, then every 6 months for 3 years	At the end of the 1st year, then at the end of the 3rd year, every 5 years thereafter	CT TAP: yearly for 5 years if high risk of recurrence
ASCO	Every 3–6 months for 2 years, then every 6 months for 3 years	Every 3–6 months for 3 years for stage II/III disease	At 1 year, then every 5 years thereafter	CT TA: annually for 3 years. Add pelvis for rectal cancer
ESMO	Every 3–6 months for 3 years, then every 6 months for 2 years	Every 3–6 months for 3 years, then every 6–12 months for 2 years	At 1 year, then every 3–5 years	CT TA every 6–12 months for 3 years if high risk. CEUS could substitute for abdominal CT scan
ASCRS	Every 3–6 months for 2 years then every 6 months for 5 years	Every 3–6 months for 2 years then every 6 months for 5 years	1 year after preoperative colonoscopy	CT TAP annually for 5 years
ICMR	Every 3 monthly in the 1st year, every 6 months until 5 years and then annually	Every 3 monthly in the 1st year, every 6 months until 5 years and then annually	At 1 year after surgery and every 3 years thereafter	CT TAP at the end of the 1st, 2nd, and 3rd year after surgery

TAP, Thorax, abdomen, and pelvis; NCCN, National Comprehensive Cancer Network; ASCO, American Society Clinical Oncology; ESMO, European Society Medical Oncology; ASCRS, American Society of Colon and Rectal Surgeons

reports and electronic medical records of 778 patients of colorectal cancer treated in our institute between August 2013 and August 2014. All operated cases of CRC treated with a curative intent were included in the study. Patients with up-front metastasis, those treated with a palliative intent, those without definite operative details, or those with no surveillance imaging details were excluded. Patients had 3 monthly serum carcinoembryonic antigen (CEA) levels, 3–6 monthly USG, and 12 monthly contrast-enhanced CT of the chest, abdomen and pelvis for surveillance as per institutional surveillance protocol. Radiology findings on the surveillance USG and CT as also serum CEA levels were noted from the electronic medical records. The imaging itself was not reviewed.

Results

Out of the 778 patients, 548 were excluded after application of the exclusion criteria with 230 patients being included for the final evaluation (Fig. 1). These included 157 males (68%) and 73 females (32%), with a median age of 42.3 years (range 16–74 years). The median follow-up time was 11 months (range 2–34 months).

77/230 (33%) patients developed recurrent disease, with the median disease-free survival being 8.6 months. 48/77 (62%) had a single site of recurrence, while 29/77 (38%) had more than one sites of recurrences. The lung (29/77) was the most common site of recurrence, followed by the liver (22/77) and peritoneum (17/77) (Table 2). Other less common sites of recurrence were the skeletal system, brain, retroperitoneal nodes, and anastomotic site. The liver was the solitary site of recurrence in 12/77 patients.

Of the 230 patients under surveillance, USG detected only five patients (2%) with liver metastases. Four of these five patients also had raised concomitant serum CEA levels, with one patient having normal serum CEA level. Three of these five patients had extrahepatic metastases as well at the time of detection and were treated with palliative intent. The remaining two (including the patient with normal serum CEA) had a solitary liver recurrence and were treated with curative intent (left hepatectomy and radiofrequency ablation respectively).

Apart from this, USG also detected three false positive lesions (all benign on image-guided sampling). There were four false-negative cases as well, in which USG failed to detect liver metastases which were subsequently detected on CT or PET/CT performed within 2 weeks of USG due to high clinical suspicion and rising CEA levels.

Fig. 1 Schematic representation of the patient selection process

Table 2 Sites of recurrent disease

Common sites of recurrence	Number of cases
Liver	22
Lung	29
Peritoneum	17
Bone	11

Discussion

The role of hepatic imaging vis-à-vis only abdominal CT scan vs. interim hepatic ultrasound for colorectal cancer surveillance is still a matter of debate in India and other developing countries. This is because of the easy availability and relative affordability of USG as compared to CT. This is despite all published guidelines not advocating the use of interim USG.

Surveillance in CRC per se for early detection of recurrence is an accepted international practice and is known to improve survival [2, 6, 7, 16–19]. Chau et al., for example, demonstrated that patients whose relapses were detected by symptoms had inferior survival compared with those detected by CT scan in a study of 530 patients [20]. Serum CEA rise is often the first signal of recurrence; a positive value can be detected 1.5–6 months before clinical detection or detection with other tests [14, 20]. However, there are false-positive rates of CEA elevation of 7–16% and false-negative rates of up to 40%. Importantly, serum CEA monitoring is also effective in patients without elevation in the preoperative setting. In these patients, a subsequent elevation can be observed in up to 44% patients with recurrent disease [14].

A systematic review of 42 studies concluded that the sensitivity of CEA lies between 50 and 80% in detecting relapses, while the specificity and negative predictive value is above 80%. Results on positive predictive value ranged from 45.8 to 95.2% and showed low reliability [18]. However, serum CEA testing alone does not show survival benefit in individual studies [21, 22]. Only trials including serum CEA testing along with liver imaging demonstrate a survival benefit.

In another similar study of 619 patients by Arriola et al. [23], 208 patients developed relapse, with the liver being the most common overall site of recurrence. Imaging techniques, including abdominopelvic CT and liver ultrasound, diagnosed relapse in only 19% of patients (as compared with 72% with CEA testing), but 50 to 60% of those cases were resectable (as compared with 32% with CEA testing). USG was the first indicator of relapse in eight cases (3.8%) of cases, of which five underwent surgery. This is comparable with the detection of hepatic recurrence by USG in 2% patients in our study.

A randomized clinical trial by Primrose et al. [24] found that intensive follow-up by either scheduled CEA or CT increased the likelihood of detecting a recurrence that can be treated with curative intent. In their study of 1202 patients,

they found no statistically significant difference in early detection of recurrences in CEA only group (11%) vs. CT only group (16.1%) vs. CEA + CT group (13.2%). It was also reported that surgical treatment of recurrence with curative intent was in only 2.3% (7/301) of the subjects in the minimum follow-up group as compared to 6.7% (20/300) in the CEA group, 8% (24/299) in the CT group, and 6.6% (20/302) in the CEA + CT group. The investigators concluded that “intensive imaging or CEA screening each provided an increased rate of surgical treatment of recurrence with curative intent compared with minimal follow-up and there was no advantage in combining CEA and CT. If there is a survival advantage to any strategy, it is likely to be small.”

Our study has some limitations. We only evaluated radiology reports and did not look at the actual images. However, USG is an operator-dependent modality and looking at the images was unlikely to help. Also, it is unlikely that all patients followed up perfectly with respect to either imaging or non-imaging follow-up, but we believe this represents the practical clinical situation. Also, ours is a tertiary cancer center, and there may be a selection bias in our cohort of patients. Other limitations include the retrospective nature of the study and the relatively small number of patients.

In conclusion, we found no significant added advantage of ultrasonography in the surveillance of patients of treated CRC. Our findings are consistent with published guidelines that routine surveillance USG should be discouraged in patients of CRC.

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