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Impact of liver-directed therapy in colorectal cancer liver metastases



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ABSTRACT

Background: There is a paucity of data on the current management and outcomes of liverdirected therapy (LDT) in older patients presenting with stage IV colorectal cancer (CRC). The aim of the study was to evaluate treatment patterns and outcomes in use of LDT in the setting of improved chemotherapy.

Methods: We used Cancer Registry and linked Medicare claims to identify patients aged \geq 66 y undergoing surgical resection of the primary tumor and chemotherapy after presenting with stage IV CRC (2001–2007). LDT was defined as liver resection and/or ablation-embolization. *Results*: We identified 5500 patients. LDT was used in 34.9% of patients; liver resection was performed in 1686 patients (30.7%), and ablation-embolization in 554 patients (10.1%), with 322 patients having both resection and ablation-embolization. Use of LDT was negatively associated with increasing year of diagnosis (odds ratio [OR] = 0.96, 95% confidence interval [CI] 0.93–0.99), age >85 y (OR = 0.61, 95% CI 0.45–0.82), and poor tumor differentiation (OR = 0.73, 95% CI 0.64–0.83). LDT was associated with improved survival (median 28.4 *versus* 21.1 mo, *P* < 0.0001); however, survival improved for all patients over time. We found a significant interaction between LDT and period of diagnosis and noted a greater survival improvement with LDT for those diagnosed in the late (2005–2007) period.

Conclusions: Older patients with stage IV CRC are experiencing improved survival over time, independent of age, comorbidity, and use of LDT. However, many older patients deemed to be appropriate candidates for resection of the primary tumor and receipt of systemic chemotherapy did not receive LDT. Our data suggest that improved patient selection may be positively impacting outcomes. Early referral and optimal selection of patients for LDT has the potential to further improve survival in older patients presenting with advanced colorectal cancer.

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1. Introduction

Metastatic disease is present at the time of diagnosis in 20% of patients presenting with colorectal cancer (CRC), and for these

patients, the liver is the most common site of metastatic disease [1,2]. Advances in chemotherapeutic regimens, surgical technique, and postoperative care have allowed for aggressive treatment of liver metastases in patients who

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previously would have only been candidates for palliative chemotherapy. Liver resection is the only potentially curative option and the preferred treatment modality in patients with isolated and resectable liver metastases. However, resection may not be possible in the case of multiple metastases, extensive bilobar disease, or in patients who are poor surgical candidates. When resection is not possible, liver ablation or chemoembolization are alternative techniques to decrease tumor burden and prolong survival [3]. Treatment with aggressive multimodality therapy has led to 5-y survival rates exceeding 50% for select patients [4].

There is a paucity of data on the current management and outcomes in older patients presenting with CRC liver metastases. In the setting of metastatic disease at presentation, the management of liver metastases is especially challenging and the benefit of liver-directed therapy (LDT) in the setting of modern chemotherapy is not as clear. Although single institution retrospective studies from specialized centers have demonstrated low mortality rates in carefully selected older patients undergoing liver resection [5-12], these reports have included both synchronous and metachronous disease. In addition, the effects of ablative therapies such as radiofrequency ablation and chemoembolization on survival have not been well studied.

We used population-based data to evaluate the use of liver resection, ablation, and chemoembolization (LDT) in older patients presenting with metastatic CRC in the era of more effective oxaliplatin- and irinotecan-containing chemotherapeutic regimens [13–15]. We specifically evaluated time trends in the use of these modalities and, when used, the timing of LDT in relation to treatment of the primary tumor and receipt of systemic therapy. Finally, we evaluated the effects of these therapies on long-term survival.

2. Methods

This study was deemed to be exempt from review by the Institutional Review Board at the University of Texas Medical Branch.

2.1. Data source

We used Texas Cancer Registry (TCR)- and Surveillance Epidemiology and End Results (SEER)-linked Medicare data from 2000–2009. SEER and TCR collect data on all cancer cases covered by the respective registries. Data collected include patient demographics, primary tumor site, stage, first course of treatment, tumor morphology, cause of death, and survival [16,17]. All cancer-related variables included in the analysis were identical between the two registries. The Center for Medicare and Medicaid Services performed the Medicare linkage for both data sets. Approximately 98% of all people aged >65 y in TCR and 93% in SEER can be linked with Medicare enrollment and claims files [18,19]. The Medicare claims data include billing information on hospital stays, physician services, and hospital outpatient visits [20]. For this study, data were extracted from the Medicare Denominator file (demographics and eligibility), the Medicare Provider Analysis and Review file (MEDPAR, inpatient claims), the Carrier claim file (claims from noninstitutional service providers), and the

CancerICD-0-3 histology codesAdenocarcinoma8000, 8050, 8051, 8052, 8010, 8021, 8022, 8140, 8141, 8143, 8145, 8147, 8210, 8211, 8220, 8221, 8220, 8260, 8261, 8262, 8263, 8430, 8440, 8470, 8471, 8480, 8481, 8490, 8550, 8551, 8570, 8571, 8572, 8573, 8574, and 8575TreatmentProcedure codesColorectal resectionsICD-9-CM: 45.71.45.76, 45.79, 45.81.45.83, 17.31-17.36, 17.39, 48.42-48.43, 48.49-48.52, 48.59-48.64, 48.69 CPT: 44140-44141, 44143-44147, 44150-44153, 44150, 44204-44208, 44210, 44155-44158, 45110-45114, 45116, 45110, 45123, 45120, 45160, 45170, 45171, 45172, 44120-44212, 4510, 45110, 45114, 45116, 45123, 45120, 45160, 45170, 45171, 45172, 44120-44212, 4510, 45114, 45116, 45119, 45123, 45120, 45160, 45170, 45171, 45172, 44120-44212, 4510, 45114, 45116, 45119, 45123, 45120, 45160, 45170, 45171, 45172, 44120, 44212, 4510, 45114, 45116, 45119, 45123, 45120, 45160, 45170, 45171, 45172, 44120, 44212, 4510, 45114, 45116, 45119, 45123, 45120, 45160, 45170, 45171, 45172, 44120, 44212, 4510, 45114, 45116, 45119, 45123, 45120, 45160, 45170, 45171, 45172, 44120, 44212, 4510, 45114, 45116, 4510, 45123, 45120, 45160, 45170, 45171, 45172, 44120, 44212, 4510, 45114, 45116, 45104, 55123, 45120, 45160, 45170, 45171, 45172, 44120, 44122, 45123, 45120, 451	Table 1 $-$ ICD-9 diagnosis codes used to identify CRC and treatment in patients presenting with stage IV CRC.	
Adenocarcinoma 8000, 8050, 8051, 8052, 8010, 8021, 8022, 8140, 8141, 8143, 8145, 8147, 8210, 8211, 8220, 8260, 8261, 8262, 8263, 8430, 8440, 8470, 8471, 8480, 8481, 8490, 8550, 8551, 8570, 8571, 8572, 8573, 8574, and 8575 Treatment Procedure codes Colorectal resections ICD-9-CM: 45.71-45.76, 45.79, 45.81-45.83, 17.31-17.36, 17.39, 48.42-48.43, 48.49-48.52, 48.59-48.64, 48.69 CPT: 44140-44141, 44143-44147, 44150-44153, 44160, 44204-44208, 44210, 44155-44158, 45110-45114, 45116, 45119-45121, 45124, 45126, 45160, 45170, 45171, 45172, 44120-44212, 45395, 45397 Chemotherapy ICD-9 procedure code: 99.25 ICD-9 procedure code: version 58.1, version 66.2, and version 67.2 HCPCS and CPT codes: Q0083-q0085, 51,720, J0640, 964XX, 96,400-96,549, J9000-J99999, G0355-C0363, G9021-G9032 Modern chemotherapy (oxaliplatin, irinotecan, or bevacizumab containing regimens) J9190 and J0640 Standard chemotherapy (5-FU/LV only) J9190 and J0640 Liver resections CPT: 47100, 47120, 47122, 47125, 47130 Ablation-embolization liver procedures CPT: 47370 (RFA), 47371 (cryosurgical), 47380 (open RFA), 47381 (open cryosurgical), 47380 (pen cryosurgical), 47381 (pen cryosurgical), 47380 (pen cryosurgical), 47380 (pen cryosurgical), 47381 (pen cryosurgical), 47380 (pen cryosurgical),	Cancer	ICD-O-3 histology codes
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ICD-9: 50.93-50.94	Liver chemoembolization	CPT: 37204 and 75894 ICD-9: 50.93-50.94

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