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ORIGINAL ARTICLE – COLORECTAL CANCER

Combined Proctectomy and Hepatectomy for Metastatic Rectal Cancer Should be Undertaken with Caution: Results of a National Cohort Study

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ABSTRACT

Background. Simultaneous proctectomy and hepatic resection for stage IV rectal cancer remains controversial due to concerns for increased morbidity and mortality. While small series have described simultaneous rectal and hepatic resection, surgical outcomes in a large national cohort have not been described.

Methods. Overall, 9012 patients with stage IV rectal adenocarcinoma with hepatic metastases were identified in the National Cancer Data Base (2010–2015). Associations between treatment selection, tumor and patient characteristics, 30- and 90-day mortality, and factors predictive of survival after surgery were examined. Logistic regression analyses were used to evaluate associations between tumor/patient characteristics, and selection of combined proctectomy and hepatectomy (C-PH). Kaplan–Meier analysis was used to identify median survival stratified by age and other patient-specific factors.

Results. Among patients included for analysis, 1331 (14.8%) underwent C-PH. Factors associated with lower rates of C-PH included increasing age, Black/Hispanic race, increased Charlson comorbidity score, Medicare/Medicaid/uninsured status, and treatment at a community cancer program. Thirty- and 90-day mortality increased with age (Chi square 11.4, $p < 0.005$; and Chi square 23.9, $p < 0.001$, respectively). On multivariate analysis, poorer survival after C-PH was associated with age > 70 years (hazard ratio [HR] 1.8, 95% confidence interval [CI] 1.0–2.5, $p < 0.001$), perineural invasion (HR 1.5, 95% CI 1.2–1.9, $p < 0.001$), kras mutation (HR 1.5, 95% CI 1.1–2.1, $p = 0.006$), positive circumferential margin (HR 1.3, 95% CI 1.0–1.7, $p = 0.03$), and omission of postoperative chemotherapy (HR 1.4, 95% CI 1.1–1.7, $p = 0.002$).

Conclusions. C-PH should be utilized with caution in frail, high-risk patients. Such patients may be better served by staged surgical management or nonsurgical therapy.

Of the approximately 43,000 new cases of rectal cancer in the US diagnosed annually, up to 20% will present with liver metastases.[1,2] Hepatic resection for rectal metastases is the only potentially curative treatment, with 5-year survival rates of 31–58%.[3] Over the past decades, increasing safety of hepatic resection has justified more aggressive surgical management in patients with greater burden of metastatic disease and comorbidity. Moreover, more effective chemotherapy can downstage initially unresectable patients, increasing the number of surgical candidates further.[4]

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In patients with synchronous metastases, optimal timing of hepatic resection relative to the removal of the primary tumor has not been established. Combined resection of colon tumors with hepatic metastasis is considered safe in selected populations, with morbidity, mortality and complication rates similar to those achieved with staged resection.[5,6] Indeed, selected high-volume centers have demonstrated excellent outcomes with the advantage of shorter overall length of stay and simplification of multimodality treatment sequencing. However, given more frequent application of major or extended liver resection and the increasing age and comorbidity of surgical patients, combined liver resection and colon resection may lead to serious morbidity or mortality at a frequency that is not discernable in small series of selected patients.[6]

The application of evidence drawn from the larger experience of simultaneous colon and hepatic resection to rectal cancer specifically, remains more controversial. Most studies of combined resection have been enriched for right-sided or sigmoid colon primaries. Longer operative time with proctectomy and higher risk of anastomotic leak (with low colorectal anastomosis) increase the potential for poor outcomes when performed in combination with hepatectomy. A few small institutional series at highly specialized centers have shown acceptable morbidity and mortality of combined proctectomy and hepatectomy (C-PH) in highly selected patients.[7] The aim of this study was to describe patient and hospital factors associated with C-PH, as well as perioperative morbidity and mortality, in a large national cohort.

METHODS

Data Source

After Institutional Review Board approval, data from 2010 to 2015 were identified in the rectal participant use file of the National Cancer Data Base (NCDB), a joint effort between the American Cancer Society and the American College of Surgeons' Commission on Cancer. Established in 1989, the NCDB is a nationwide, facility-based, comprehensive clinical surveillance resource oncology dataset that currently captures 70% of all newly diagnosed malignancies in the US annually.[8]

Patient Selection

Patients diagnosed with pathologic stage IV rectal cancer with liver metastasis from 2010 to 2015 were selected, as defined by the International Classification of Diseases–Oncology, Third Revision.[9] Staging was derived from the American Joint Committee on Cancer (AJCC) information provided, and separate fields coding for site of metastasis; patients with metastasis to the brain, bone, or lungs were excluded. Patients with incomplete data regarding tumor size and tumor differentiation were also excluded. Patients who underwent a C-PH were defined as those who had codes for having both a proctectomy and a simultaneous surgical resection to a distant visceral site (electronic supplementary Fig. 1). While the NCDB does not code specifically for type of visceral resection (i.e. major or minor hepatectomy), it does distinguish distant lymphadenectomy from visceral resection.

Variables

Demographic, cancer-specific, and facility-related variables available in the NCDB have been defined previously, and include demographic information, socioeconomic variables, tumor characteristics, staging, and surgery type.[8]

Statistical Methods

Descriptive statistics are displayed as frequencies for categorical variables, and medians with interquartile range for continuous variables. Univariate analysis was performed using the Chi square test or *t* test, respectively. Multivariable logistic regression was then performed to assess association between demographic/clinical factors and utilization of C-PH. Univariate and multivariable analysis was also performed to analyze predictors of survival within the C-PH cohort. Univariate and multivariate predictors of 30- and 90-day mortality were examined, excluding adjuvant chemotherapy, which we did not consider an independent variable as patients who died within 30–90 days postoperatively are unlikely to have received adjuvant chemotherapy.

The Kaplan–Meier method was used to estimate the overall survival function. Overall survival was defined as the time from diagnosis to death, with patients alive at the time of last follow-up censored. A p value < 0.05 was considered statistically significant. All statistics were performed using STATA MP.[10]

RESULTS

Predictors of Combined Proctectomy/Hepatectomy

A total of 8976 patients meeting the study criteria were identified and were included for analysis. The cohort was primarily male ($n = 5825$, 65%), 50–60 years of age ($n = 4965$, 55%) White ($n = 7020$, 78%), privately insured ($n = 3871$, 43%), and cared for at a comprehensive community cancer program ($n = 3630$, 43%). The majority of patients did not undergo C-PH ($n = 7660$, 85.3%) (Table 1).

On univariate analysis, patients who underwent C-PH were more likely to be < 50 years of age ($p < 0.001$), male ($p = 0.02$), have a Charlson–Deyo score below 2 ($p = 0.02$), private insurance ($p < 0.001$), higher income ($p < 0.001$), travel further for care ($p < 0.001$), and undergo surgery at an academic research program ($p < 0.001$). Patients with lymphovascular invasion (LVI) or perineural invasion (PNI) were more likely to undergo C-PH (Table 2).

On multivariate analysis, patient factors associated with performance of C-PH included age < 50 years (odds ratio [OR] 2.3, 95% confidence interval [CI] 1.7–3.0, $p < 0.001$), age 50–69 years (OR 1.8, 95% CI 1.4–2.2, $p < 0.001$], female sex (OR 1.2, 95% CI 1.1–1.4, $p = 0.004$), White race (OR 2.0, 95% CI 1.5–2.7, $p < 0.001$), and other race (OR 2.0, 95% CI 1.3–3.1, $p = 0.001$). Socioeconomic factors predictive of performance of C-PH included private insurance (OR 2.0, 95% CI 2.0–4.3, $p < 0.001$), Medicare (OR 2.2, 95% CI 1.43.2, $p < 0.001$), Medicaid (OR 2.0, 95% CI 1.3–3.2,

TABLE 1 Descriptive statistics [$n = 8976$]

		No C-PH [$n = 7660$ (85.3%)]	C-PH [$n = 1316$ (14.7%)]	p value
Age, years	< 50	1334 (17)	368 (28)	< 0.001
	50–69	4173 (54)	783 (59)	
	≥ 70	2153 (28)	165 (13)	
Sex	Male	5007 (65)	818 (62)	0.02
	Female	2653 (35)	498 (38)	
Race	White	5904 (77)	1116 (85)	< 0.001
	Black	840 (11)	68 (5.2)	
	Hispanic	545 (7.1)	60 (4.6)	
	Other	322 (4.2)	62 (4.7)	
	Unknown	49 (0.6)	10 (0.8)	
Charlson–Deyo	0	6116 (80)	1051 (80)	0.02
	1	1146 (15)	218 (17)	
	2+	398 (5.2)	47 (3.6)	
Insurance	Private	3067 (40)	804 (61)	< 0.001
	Medicare	2992 (39)	321 (24)	
	Uninsured	531 (6.9)	37 (2.8)	
	Medicaid	846 (11)	116 (8.8)	
	Unknown	224 (2.9)	38 (2.9)	
Facility type	Community cancer	917 (13)	66 (5.4)	< 0.001
	Comprehensive community cancer	3235 (44)	395 (32)	
	Academic/research	2469 (34)	656 (54)	
	Integrated cancer network	694 (9.5)	99 (8.1)	
Income, US$	< 38,000	1477 (19)	187 (14)	< 0.001
	38,000–47,999	1902 (25)	308 (23)	
	48,000–63,000	2019 (27)	363 (28)	
	> 63,000	2211 (29)	453 (35)	
Distance from facility, miles	< 4.4	2010 (26.3)	195 (14.8)	< 0.001
	4.4–9.9	1982 (25.9)	270 (20.5)	
	10.0–24.5	1896 (24.8)	338 (25.7)	
	> 24.5	1766 (23.1)	512 (38.9)	
LVI	Present	752 (9.8)	440 (33.4)	< 0.001
PNI	Present	470 (6.1)	330 (25.1)	< 0.001
KRAS [mutation +]	Present	856 (11.2)	801 (60.9)	< 0.001

Data are expressed as n (%)

C-PH combined proctectomy and hepatectomy, *LVI* lymphovascular invasion, *PNI* perineural invasion

TABLE 2 Predictors of combined proctectomy and hepatectomy

		Univariate		Multivariate	
		OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age, years	< 50	3.6 (2.6–4.4)	< 0.001	2.3 (1.7–3.0)	< 0.001
	50–69	2.5 (2.1–2.9)	< 0.001	1.8 (1.4–2.2)	< 0.001
	≥ 70	Ref		Ref	
Sex	Male	Ref		Ref	
	Female	1.2 (1.0–1.3)	0.05	1.2 (1.1–1.4)	0.004
Race	Black	Ref		Ref	
	White	2.3 (1.8–3.0)	< 0.001	2.0 (1.5–2.7)	< 0.001
	Hispanic	1.4 (1.0–2.0)	0.1	1.3 (0.9–2.0)	0.2
	Other	2.4 (1.6–3.4)	< 0.001	2.0 (1.3–3.1)	0.001
	Unknown	2.5 (1.2–5.2)	0.01	1.8 (0.8–4.3)	0.2
Charlson–Deyo	0	1.5 (1.1–2.0)	0.02		
	1	1.6 (1.1–2.3)	0.005		
	2+	Ref			
Insurance	Uninsured	Ref		Ref	
	Private	3.8 (2.7–5.3)	< 0.001	2.0 (2.0–4.3)	< 0.001
	Medicare	1.5 (1.1–2.2)	0.02	2.2 (1.4–3.2)	< 0.001
	Medicaid	2.0 (1.3–2.9)	0.001	2.0 (1.3–3.2)	0.001
	Unknown	2.4 (1.5–3.9)	< 0.001	2.1 (1.2–3.7)	0.007
Facility type	Community cancer	Ref		Ref	
	Comprehensive community cancer	1.7 (1.3–2.2)	< 0.001	1.1 (1.1–1.8)	0.03
	Academic/research	3.7 (2.8–4.8)	< 0.001	2.9 (2.2–3.9)	< 0.001
	Integrated cancer network	2.0 (1.4–2.7)	< 0.001	1.6 (1.1–2.3)	0.006
Income, US$	< 38,000	Ref			
	38,000–47,999	1.3 (1.1–1.6)	0.01		
	48,000–63,000	1.4 (1.2–1.7)	< 0.001		
	> 63,000	1.6 (1.2–1.9)	< 0.001		
Distance from treatment facility, miles	< 4.4	Ref		Ref	
	4.4–9.9	1.4 (1.2–1.7)	0.001	1.2 (0.9–1.5)	0.1
	10.0–24.5	1.8 (1.5–2.2)	< 0.001	1.3 (1.0–1.6)	0.02
	> 24.5	3.0 (2.5–3.6)	< 0.001	1.8 (1.3–2.2)	< 0.001
LVI [present]		1.4 (1.2–1.7)	< 0.001	1.3 (1.1–1.4)	0.005
PNI [present]		2.1 (1.8–2.5)	< 0.001	1.3 (1.1–1.6)	0.004
KRAS [mutation +]		0.9 (0.7–1.1)	0.1		

OR odds ratio, *CI* confidence interval, *LVI* lymphovascular invasion, *PNI* perineural invasion

$p = 0.001$), or uninsured status (OR 2.1, 95% CI 1.2–3.7, $p = 0.007$). Treatment at a facility other than a community cancer program was associated with higher odds of receiving a C-PH; this was strongest for academic/research programs (OR 2.9, 95% CI 2.2–3.9, $p < 0.001$). Increasing the distance from home to the treatment facility was also predictive of an increased rate of C-PH, which was strongest above 24.5 miles (OR 1.8, 95% CI 1.3–2.2, $p < 0.001$). The presence of both LVI (OR 1.3, 95% CI 1.1–1.4, $p = 0.005$) and PNI (OR 1.3, 95% CI 1.1–1.6, $p = 0.004$) was associated with C-PH (Table 2).

Predictors of Short-Term Survival After Combined Proctectomy/Hepatectomy

Overall 30- and 90-day mortality following C-HP was 0.92% and 2.12%, respectively. Stratified by age, 30- and 90-day mortality increased with age (Chi square 11.4, $p < 0.005$; and Chi square 23.9, $p < 0.001$, respectively) (Table 3). Among the 1316 patients who underwent a C-HP, univariate predictors of 30-day mortality included age > 70 years, Medicare insurance, and omission of neoadjuvant chemotherapy. On multivariate analysis, only

TABLE 3 Age-stratified long- and short-term survival after combined proctectomy and hepatectomy

	30-day mortality (%)	90-day mortality (%)	Median survival (months)
Overall	0.92	2.12	51.1
Age, years			
< 50	0.32	0.63	54.7
50–69	0.65	1.62	51.1
70+	3.34	7.38	37.2

the omission of neoadjuvant chemotherapy remained significantly associated with 30-day mortality. Univariate predictors of 90-day mortality included age ≥ 70 years, Charlson–Deyo score of 1, Medicare insurance, positive circumferential margin, and omission of neoadjuvant chemotherapy. Multivariate predictors of 90-day mortality included age ≥ 70 years, Charlson–Deyo comorbidity condition (CDCC) of 1, and omission of neoadjuvant chemotherapy. Race, sex, household income, facility type, and pathologic tumor characteristics (LVI, PNI, KRAS status) were nonpredictive of both 30- and 90-day mortality (Table 4).

Predictors of Long-Term Survival After Combined Proctectomy/Hepatectomy

After omission of patients with 90-day mortality, median overall survival after C-PH was 51.6 months. Stratified by age, median overall survival following C-PH was 54.8, 51.6, and 39.4 months, for patients aged < 50, 50–69, and ≥ 70 years, respectively (electronic supplementary Fig. 2). Univariate predictors of poorer survival included age > 70 years, CDCC of 1, Medicare and uninsured status, LVI of the primary tumor, PNI of the primary tumor, KRAS mutation, positive circumferential resection margin, omission of neoadjuvant chemo/radiotherapy, and omission of adjuvant chemotherapy. Sex, race, income, facility type, and microsatellite instability status were nonpredictive. On multivariate analysis, age > 70 years, PNI, KRAS mutation, positive resection margin, and omission of perioperative chemotherapy were predictive of poorer survival after C-PH (Table 5).

DISCUSSION

The present study, from a large national cohort, demonstrates that C-PH can be performed safely in younger, properly selected patients, with acceptable perioperative mortality, but should be undertaken with caution in frail patients with high-risk tumor features. It also

TABLE 4 Predictors of 30- and 90-day mortality among combined proctectomy and hepatectomy patients

		30-day mortality				90-day mortality			
		Univariate		Multivariate		Univariate		Multivariate	
		OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Age, years	< 50	Ref				Ref		Ref	
	50–69	2.0 (0.2–18.3)	0.6			2.6 (0.5–11.8)	0.2	2.1 (0.4–9.8)	0.3
	≥ 70	10.9 (1.3–94.2)	0.03			12.5 (2.7–57.0)	0.001	8.5 (1.8–40.1)	0.007
Charlson–Deyo	0					Ref		Ref	
	1					3.6 (1.5–8.5)	0.004	2.1 (1.1–6.9)	0.02
	2+					1.6 (0.2–13.2)	0.6	0.9 (0.1–7.8)	0.9
Insurance	Private	Ref				Ref			
	Medicare	8.7 (1.8–41.9)	0.007			5.9 (2.2–15.5)	<0.001		
Circumferential resection margin (colon) positive						3.5 (1.2–10.2)	0.02		
Omission of neoadjuvant chemotherapy		5.4 (1.4–19.3)	0.009	5.4 (1.4–19.3)	0.009	4.0 (1.7–9.2)	0.001	3.0 (1.3–7.2)	0.01

OR odds ratio, *CI* confidence interval highlights disparities in access to care, with decreased C-PH in non-White as well as uninsured, Medicare, and Medicaid patients.

C-PH combines two major operations associated with discreet physiologic challenges. Previous studies, risk-stratifying combined hepatic resection and colon resection, demonstrated increased morbidity and mortality with extended colon resection and major hepatic resection (formal right or left hepatectomy), particularly in elderly patients. Tzeng et al. reported a 2% 30-day mortality in patients < 75 years of age, compared with 4.8% in those > 75 years of age, after combined colon resection and hepatectomy, however these mortality rates were as high as 10% in patients > 75 years of age who had a right or extended hepatectomy.[6] In addition, multiple Surveillance, Epidemiology, and End Results (SEER) Medicare analyses demonstrated poorer short- and long-term survival with increasing age and synchronous hepatic and colonic resection.[11,12] Robertson et al. reported 90-day mortality rates of 8.7% for patients 75–79 years of age, and 15.8 for those > 80 years of age, as well as poorer long-term survival with increasing age and synchronous resection on multivariate analysis.[12] Age in these studies, as well as in the present study, is likely a surrogate for frailty.[13]

Few large studies have evaluated the safety and outcomes of combined proctectomy and hepatic resection. Our results are similar to data from studies including colon resection. Our study confirms that while combined proctectomy and hepatic resection is associated with low postoperative mortality in younger patients, mortality increases significantly with age. In our cohort, age > 70 years was a significant independent predictor of 90-day mortality and the strongest predictor of long-term survival after C-PH, although this may be confounded by increasing general mortality with increasing age.

The genetic profile of the tumor, the rates of local disease control, and administration of pre- and postoperative chemotherapy all affect short- and long-term survival after C-PH. Failure of local control, as evidenced by a positive circumferential margin, also leads to poorer long-term survival, as has been shown previously in nonmetastatic rectal cancer.[14] These variables may be a surrogate for lower-quality care or lack of multidisciplinary planning, ultimately accounting for high rates of morbidity and mortality, as has been suggested previously in studies of the volume–outcome relationship in rectal cancer.[15] Notably, a surgery-first approach (omission of neoadjuvant chemotherapy) is predictive of poorer long- and short-term survival. This finding affirms that notion that chemotherapy

TABLE 5 Predictors of worse survival among combined proctectomy and hepatectomy patients

		Univariate		Multivariate	
		HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age, years	< 50	Ref		Ref	
	50–69	1.1 (0.9–1.4)	0.5	1.1 (0.9–1.3)	0.6
	≥ 70	1.8 (1.3–2.4)	< 0.001	1.8 (1.3–2.5)	<0.001
Charlson–Deyo	0	Ref			
	1	1.3 (1.0–1.7)	0.03		
	2	1.3 (0.8–2.1)	0.3		
Insurance	Private	Ref			
	Medicare	1.5 (1.2–1.8)	0.001		
	Medicaid	1.0 (0.7–1.5)	0.9		
	Uninsured	1.7 (1.1–2.7)	0.03		
	Unknown	0.7 (0.3–1.5)	0.3		
LVI		1.3 (1.1–1.6)	0.02		
PNI		1.6 (1.3–2.0)	< 0.001	1.5 (1.2–1.9)	<0.001
KRAS		1.5 (1.1–2.0)	0.007	1.5 (1.1–2.1)	0.006
Circumferential resection margin (colon) positive		2.1 (1.7–2.7)	< 0.001	2.1 (1.6–2.7)	<0.001
Omission of neoadjuvant chemotherapy		1.2 (1.0–1.5)	0.03	1.3 (1.0–1.7)	0.03
Omission of neoadjuvant radiotherapy		1.2 (0.9–1.7)	0.2		
Omission of adjuvant chemotherapy		1.3 (1.0–1.6)	0.04	1.4 (1.1–1.7)	0.002

HR hazard ratio, *CI* confidence interval, *LVI* lymphovascular invasion, *PNI* perineural invasion is an effective selection tool for surgery, as has been suggested in some smaller retrospective and prospective studies.[16]

Previous studies have demonstrated poorer access to colon cancer surgery based on race and socioeconomic factors. Multiple large studies have shown that African Americans have decreased access to definitive cancer surgery and sphincter-preserving options.[17] Similar disparities in access to care and outcomes in colorectal cancer exist for uninsured/Medicaid and low-income patients.[17,18] The present series demonstrates that Black and Hispanic patients, as well as those with nonprivate insurance and lower income, have decreased the rates of C-PH. The explanation for these disparities to care are likely multifactorial and may include differences in provider referral to care or patient willingness to undergo major cancer operations.[19–21] This series also demonstrates that C-PH is performed more often at academic centers. However, while this may again represent desperate access to academic centers, it more likely represents an increased concentration of specialized resources required for the complex care and decision making for these patients. This may also explain the higher rates of C-PH for patients who travel for care, with patients seeking out surgical intervention at further yet more specialized centers. Previous work has demonstrated improved outcomes in major hepatic surgery at academic and high-volume centers.[22] Despite this, we were not able to identify any associations between medical center type and both 30- and 90-day mortality, either representing that these disparities do not exist or, more likely, that a more nuanced analysis, including length of stay, morbidity/complication rate, and oncologic outcomes, is needed.

There are several limitations in the current study that bear emphasis. First, despite efforts to ensure data quality and accuracy, retrospective data are subject to omitted entries and coding errors. As acknowledged in the Methods section, we postulated that patients who had liver metastases, who were undergoing proctectomy and resection to a distant site, were most likely undergoing a surgical hepatectomy. Despite this, it is conceivable that our cohort includes resection of other metastatic sites, without hepatectomy, although we suspect this is a low value. Additionally, important data on frailty are missing from the dataset and makes it impossible to discern the effects of frailty on the outcomes attributed to age in this dataset. Next, the NCDB does not capture the type of liver operation performed. No distinction is made regarding the extent of resection (i.e. major vs. minor hepatic resection). This represents a significant limitation and precludes assessment of the impact of extent of liver resection on morbidity. The likely enrichment of the present series with minor hepatic resections underscores the significant risk associated with any combined procedure involving proctectomy. The risk associated with proctectomy combined with major hepatectomy specifically is likely higher than that in the studied cohort. In addition, the NCDB does not capture additional forms of liver-directed therapy, including chemoembolization or radiofrequency ablation, which could also be important as a predictor of survival. The NCDB does not also capture patients who had staged proctectomy and hepatectomy, and adding this comparative cohort would be informative for analysis. However, we are only trying to demonstrate the comparative safety of C-PH in this study and to highlight high-risk groups who may not do well after this operation. We are not attempting to determine the efficacy of this approach compared with a staged approach, although agree this would be an important comparison group that would control for potentially unresectable disease. In addition, the NCDB does not capture how low a rectal anastomosis was performed, or whether a diverting loop ileostomy was performed. Inclusion of these data may lead to a more granular understanding of which procedures carry a lower risk in more elderly/frail patients. Finally, the NCDB does not capture disease-specific survival, and only reports overall survival. Again, however, we are not attempting to compare one therapy with another in this study. The overall survival metric allows us to identify patients who have limited long-term survival following C-PH. This information may temper the consideration of C-PH in these patients with limited long-term survival.

CONCLUSIONS

This series affirms that C-PH can be performed safely, with relatively low 30- and 90-day mortality rates and reasonable long-term overall survival. Despite this, we demonstrated significant disparity in use of this approach. Minority and low-income patients, as well as those with nonprivate insurance, undergo C-PH significantly less frequently than White, high-income, privately insured patients. Additionally, patients treated at academic cancer centers are much more likely to undergo C-PH than patients treated at community cancer centers. Given the potential for significant success and the low perioperative mortality associated with C-PH, providers should refer patients to higher levels of care, when appropriate, so they can be evaluated for surgical intervention. However, we also demonstrate that both short- and long-term outcomes are significantly worse in patients > 70 years of age. In addition, patients who did not receive neoadjuvant chemotherapy, as well as those with KRAS mutation or PNI/LVI, have poorer long-term survival after C-PH. For frail patients > 70 years of age with these concerning features, it may be that a more measured approach using neoadjuvant chemoradiotherapy, as well as stringent patient selection, prior to consideration of C-PH is warranted. Ultimately, combining these factors and creating a risk-stratification scoring system in a prospective study would allow the identification of patients for whom C-PH is a reasonable approach.

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