

Supplementary Methods

Multiple Imputation

We performed multiple imputation by using the PROC MI procedure in SAS version 9.4 (SAS Institute, Cary, NC) by using a Markov Chain Monte Carlo method that assumes multivariate normality for the distribution of laboratory values and an arbitrary missingness pattern. The lab values ALT, AST, and creatinine were log-transformed to approximate the normality in the imputation process, and then imputed values were transformed back to their original scales for further data analysis. We also included

the survival outcomes in the multiple imputation procedure, which would yield more valid results than multiple imputation without survival.²⁸ In total, 10 completed data sets were imputed, and on each data set we performed the Cox proportion-hazards regression analyses, the parameter estimates of which (ie, hazard ratios) were combined by using the PROC MIANALYZE procedure to incorporate missing-data uncertainty. Three statistics of assessing discrimination, including Harrell C statistic, integrated IDI, and category-free NRI were summarized by taking the average values of the 10 imputed sets. The basic summaries of demographics and clinical values were based on 1 of 10 imputed sets, and the between-imputation variations were minimal (data not presented).

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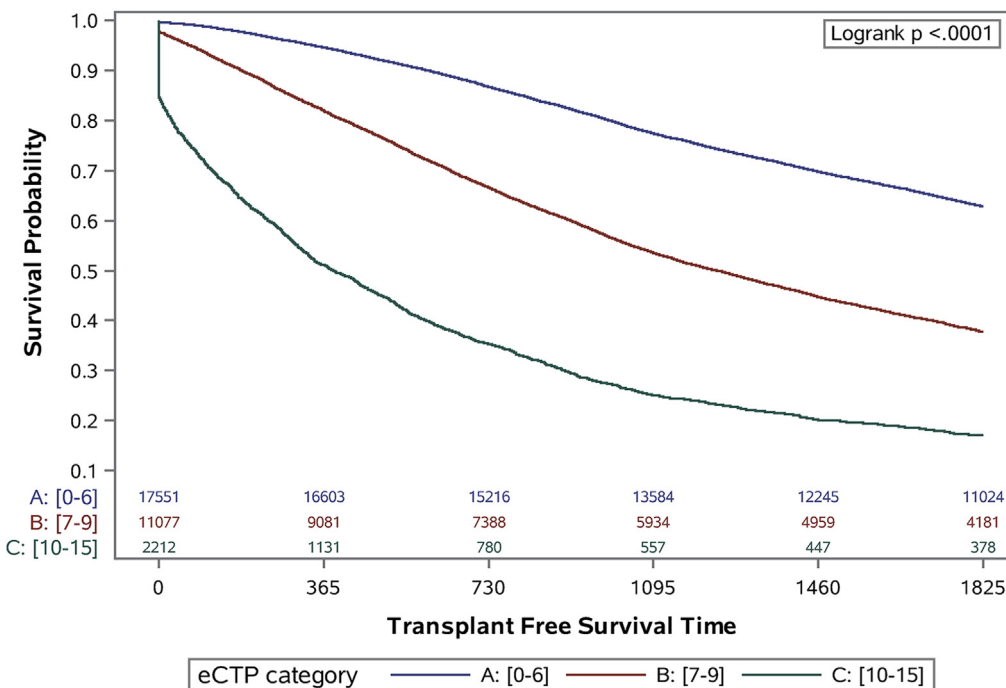
Supplementary

Figure 1. Comparison of eCTP with chart-extracted CTP assignments. (A) Cohort of HCC patients with complete data in assigned quarter (N = 80). (B) Cohort of cirrhotic patients with complete data in the assigned quarter (N = 56).

		HCC Cohort (N=80 with complete data)							
		electronic CTP							
		5	6	7	8	9	10	11	12
chart CTP	5	22	2	1	0	0	0	0	0
	6	8	19	2	0	0	0	0	0
	7	1	4	6	2	0	0	0	0
	8	0	1	2	3	1	0	0	0
	9	0	0	0	0	2	1	0	0
	10	0	0	0	1	0	0	0	0
	11	0	0	0	0	0	0	1	0
	12	0	0	0	0	0	0	0	1

		Cirrhosis Cohort (N=56 with complete data)							
		electronic CTP							
		5	6	7	8	9	10	11	12
chart CTP	5	21	3	1	0	0	0	0	0
	6	3	11	1	0	0	0	0	0
	7	0	2	2	1	0	0	0	0
	8	0	0	0	0	0	1	0	0
	9	0	0	0	2	3	1	0	0
	10	0	0	0	1	1	1	0	0
	11	0	0	0	0	0	0	0	0
	12	0	0	0	0	0	0	1	0

Kaplan-Meier Survival Curve
With Number of Subjects at Risk



Supplementary

Figure 2. Kaplan-Meier survival curve for 5-year TFS by eCTP class. eCTP A (5-6) shown in blue, B (7-9) in red, and C (10-15) in green.

Supplementary Table 1. Data Elements and Algorithm for Calculation of eCTP Ascites Subscore

Domain	Variable	Logic
CPT	LVPPRE6CNT	Count of large volume paracentesis (LVP, CPT 49082) in 6 months before index date
	LVPPOST1CNT	Count of large volume paracentesis (LVP, CPT 49082) in 1 month after index date
	TIPSSPREOTPT	Count of transjugular intrahepatic shunt (CPT 37182 or 37183) preceding index date
Pharmacy	SPIR1PRE3	Any 30-day fill of spironolactone in 3 months before index date
	SPIR3PRE3	Any 3 × 30-day or 1 × 90-day fill of spironolactone in 3 months before index date
	SPIR1POST1	Any 30- or 90-day fill of spironolactone within the month after diagnosis
	FUR1PRE3	Any 30-day fill of furosemide in 3 months before index date
	FUR3PRE3	Any 3 × 30-day or 1 × 90-day fill of furosemide in 3 months before index date
	FUR1POST1	Any 30- or 90-day fill of furosemide within the month after diagnosis
	AMIL1PRE3	Any 30-day fill of amiloride in 3 months before index date
	AMIL3PRE3	Any 3 × 30-day or 1 × 90-day fill of amiloride in 3 months before index date
	AMIL1POST1	Any 30- or 90-day fill of amiloride within the month after diagnosis
ICD9	ASCPRE6INPT	ICD9-CM code for ascites (789.5x) during inpatient visit in 6 months before index date
	ASCPPOST1INPT	ICD9-CM code for ascites (789.5x) during inpatient visit in 1 month after HCC diagnosis
	ASCPRE6OTPT	ICD9-CM code for ascites (789.5x) during outpatient visit in 6 months before index date
	ASCPPOST1OTPT	ICD9-CM code for ascites (789.5x) during outpatient visit in 1 month after HCC diagnosis
	SBPPRE6INPT	ICD9-CM code for spontaneous bacterial peritonitis (567.9) during inpatient visit in 6 months before index date
	HRSPRE6INPT	ICD9-CM code for hepatorenal syndrome (572.4) during inpatient visit in 6 months before index date
	SBPPRE6OTPT	ICD9-CM code for spontaneous bacterial peritonitis (567.9) during outpatient visit in 6 months before index date
	HRSPRE6OTPT	ICD9-CM code for hepatorenal syndrome (572.4) during outpatient visit in 6 months before index date
Ascites score = 3	LVPPRE6CNT is > 1 OR (LVPPOST1CNT = 1 and LVPPRE6CNT = 1) OR SBPPRE6INPT = 1 OR SBPPRE6OTPT = 1 OR HRSPRE6INPT = 1 OR HRSPRE6OTPT = 1 OR TIPSSPREOTPT = 1	
Ascites score = 2	Criteria for ascites score 3 not met AND	Algorithm 1 (any diuretic fill, not including furosemide): LVPPRE6CNT = 1 OR LVPPOST1CNT = 1 OR ASCPOST1INPT = 1 OR ASCPOST1OTPT = 1 OR ASCPRE6INPT = 1 OR ASCPRE6OTPT = 1 OR SPIR1POST = 1 OR SPIR1PRE3 = 1 OR AMIL1POST = 1 OR AMIL1PRE3 = 1 Algorithm 2 (3-month fill, not including furosemide): LVPPRE6CNT = 1 OR LVPPOST1CNT = 1 OR ASCPOST1INPT = 1 OR ASCPOST1OTPT = 1 OR ASCPRE6INPT = 1 OR ASCPRE6OTPT = 1 OR SPIR1POST = 1 OR SPIR1PRE3 = 1 OR AMIL1POST = 1 OR AMIL1PRE3 = 1 Algorithm 3 (any fill, including furosemide): LVPPRE6CNT = 1 OR LVPPOST1CNT = 1 OR ASCPOST1INPT = 1 OR ASCPOST1OTPT = 1 OR ASCPRE6INPT = 1 OR ASCPRE6OTPT = 1 OR SPIR1POST = 1 OR SPIR1PRE3 = 1 OR AMIL1POST = 1 OR AMIL1PRE3 = 1 Algorithm 4 (3-month fill, including furosemide): LVPPRE6CNT = 1 OR LVPPOST1CNT = 1 OR ASCPOST1INPT = 1 OR ASCPOST1OTPT = 1 OR ASCPRE6INPT = 1 OR ASCPRE6OTPT = 1 OR SPIR1POST1 = 1 OR SPIR3PRE3 = 1 OR AMIL1POST1 = 1 OR AMIL3PRE3 = 1 OR FUR1POST1 = 1 OR FUR3PRE3 = 1
Ascites score = 1	Criteria for ascites score 3 and score 2 not met	

Supplementary Table 2. Data Elements and Algorithm for Calculation of eCTP Encephalopathy Subscore

Domain	Variable	Logic
Pharmacy	LAC1PRE3	Any 30-day fill of lactulose in 3 months before index date
	LAC3PRE3	Any 3 × 30-day or 1 × 90-day fill of lactulose in 3 months before index date
	LAC1POST1	Any 30- or 90-day fill of lactulose within the month after diagnosis
	RIF1PRE3	Any 30-day fill of rifaximin in 3 months before index date
	RIF3PRE3	Any 3 × 30-day or 1 × 90-day fill of rifaximin in 3 months before index date
ICD9	RIF1POST1	Any 30- or 90-day fill of rifaximin within the month after diagnosis
	HEPRE6INPT	ICD9-CM code for Hepatic Encephalopathy (572.2x) during inpatient visit in 6 months before index date
	HEPOST1INPT	ICD9-CM code for Hepatic Encephalopathy (572.2x) during inpatient visit in 1 month after HCC diagnosis
	HEPRE6OTPT	ICD9-CM code for Hepatic Encephalopathy (572.2x) during outpatient visit in 6 months before index date
	HEPOST1OTPT	ICD9-CM code for Hepatic Encephalopathy (572.2x) during outpatient visit in 1 month after HCC diagnosis
Encephalopathy score = 3	HEPRE6INPT + HEPOST1INPT > 1	
Encephalopathy score = 2	Criteria for Encephalopathy score 3 not met AND	Algorithm 1: LAC1PRE3 = 1 OR RIF1PRE3 = 1 OR LAC1POST1 = 1 OR RIF1POST1 = 1 OR HEPRE6OTPT = 1 OR HEPOST1OTPT = 1
		Algorithm 2: LAC3PRE3 = 1 OR RIF3PRE3 = 1 OR LAC1POST1 = 1 OR RIF1POST1 = 1 OR HEPRE6OTPT = 1 OR HEPOST1OTPT = 1
Encephalopathy score = 1	Criteria for Encephalopathy score 3 and score 2 not met	

Supplementary Table 3. Cox Regression and Harrell's C Statistic for Individual Predictive Models of 1- to 4-year TFS

Variables	1-year TFS			2-year TFS		
	Summary statistic Adjusted HR (95% CI)	P value	Harrell's C statistic	Summary statistic Adjusted HR (95% CI)	P value	Harrell's C statistic
eCTP (first quarter 2008) ^a	1.63 (1.60–1.65)	<.0001	0.756 (0.005)	1.52 (1.50–1.54)	<.0001	0.717 (0.003)
VACS (change to 10 unit)	1.39 (1.38–1.41)	<.0001	0.702 (0.005)	1.34 (1.32–1.35)	<.0001	0.679 (0.003)
MELD ^a	1.11 (1.10–1.11)	<.0001	0.670 (0.005)	1.08 (1.08–1.09)	<.0001	0.645 (0.003)
CDI ^a	1.51 (1.48–1.54)	<.0001	0.671 (0.005)	1.42 (1.41–1.44)	<.0001	0.645 (0.003)
Variables	3-year TFS			4-year TFS		
	Summary statistic Adjusted HR (95% CI)	P value	Harrell's C statistic	Summary statistic Adjusted HR (95% CI)	P value	Harrell's C statistic
eCTP (first quarter 2008) ^a	1.45 (1.44–1.47)	<.0001	0.698 (0.003)	1.42 (1.40–1.43)	<.0001	0.686 (0.003)
VACS (change to 10 unit)	1.30 (1.29–1.31)	<.0001	0.667 (0.003)	1.28 (1.28–1.29)	<.0001	0.661 (0.003)
MELD ^a	1.07 (1.07–1.08)	<.0001	0.633 (0.003)	1.07 (1.06–1.07)	<.0001	0.626 (0.003)
CDI ^a	1.37 (1.35–1.38)	<.0001	0.631 (0.003)	1.34 (1.33–1.36)	<.0001	0.624 (0.003)

CI, confidence interval; HR, hazard ratio.

^aAdjusted for age and gender.

Supplementary Table 4. Incremental Value of NRI and IDI for New Predictor of 5-year TFS

Quarter	NRI		IDI	
	Estimate (95% CI)	P value	Estimate (95% CI)	P value
Q1 2008				
eCTP	0.280 (0.269–0.290)	<.001	0.109 (0.103–0.115)	<.001
VACS	0.244 (0.233–0.255)	<.001	0.091 (0.085–0.096)	<.001
MELD	0.160 (0.149–0.170)	<.001	0.042 (0.038–0.046)	<.001
CDI	0.170 (0.160–0.179)	<.001	0.049 (0.045–0.053)	<.001
CirCom Index	0.079 (0.070–0.091)	<.001	0.021 (0.018–0.024)	<.001
Q2 2008				
eCTP	0.279 (0.267–0.289)	<.001	0.111 (0.105–0.117)	<.001
VACS	0.240 (0.229–0.250)	<.001	0.088 (0.082–0.094)	<.001
MELD	0.156 (0.145–0.166)	<.001	0.041 (0.037–0.045)	<.001
CDI	0.184 (0.173–0.194)	<.001	0.053 (0.049–0.058)	<.001
CirCom Index	0.086 (0.076–0.097)	<.001	0.022 (0.019–0.025)	<.001
Q3 2008				
eCTP	0.291 (0.279–0.301)	<.001	0.118 (0.112–0.124)	<.001
VACS	0.241 (0.229–0.251)	<.001	0.090 (0.085–0.096)	<.001
MELD	0.178 (0.168–0.188)	<.001	0.048 (0.044–0.052)	<.001
CDI	0.181 (0.171–0.190)	<.001	0.051 (0.047–0.055)	<.001
CirCom Index	0.079 (0.070–0.093)	<.001	0.020 (0.017–0.023)	<.001
Q4 2008				
eCTP	0.292 (0.282–0.303)	<.001	0.117 (0.111–0.123)	<.001
VACS	0.253 (0.242–0.263)	<.001	0.095 (0.089–0.101)	<.001
MELD	0.161 (0.150–0.172)	<.001	0.046 (0.042–0.050)	<.001
CDI	0.187 (0.177–0.197)	<.001	0.053 (0.049–0.057)	<.001
CirCom Index	0.097 (0.075–0.123)	<.001	0.019 (0.017–0.022)	<.001

NOTE. Summaries were computed from average results of 10 imputed data sets.

Supplementary Table 5. Sub-hazard Ratios and Overall Fit of eCTP, MELD, and VACS in Competing Risk Regression Models

Model	Quarter	n	Events	Sub-hazard for transplant	Sub-hazard for death	Harrell's C statistic	Fine and Gray ^a
eCTP	2008Q1	60,436	15,309	1.64 (1.57–1.71)	1.49 (1.48–1.51)	0.697 ± 0.003	6315
MELD	2008Q1	60,436	15,309	1.11 (1.09–1.12)	1.09 (1.08–1.09)	0.645 ± 0.003	3151
VACS ^b	2008Q1	60,436	15,309	1.44 (1.39–1.49)	1.33 (1.32–1.34)	0.677 ± 0.003	5455
eCTP	2008Q2	62,066	15,536	1.66 (1.59–1.74)	1.48 (1.47–1.50)	0.690 ± 0.003	5931
MELD	2008Q2	62,066	15,536	1.11 (1.09–1.12)	1.08 (1.08–1.08)	0.636 ± 0.003	2763
VACS ^b	2008Q2	62,066	15,536	1.45 (1.40–1.49)	1.31 (1.30–1.32)	0.669 ± 0.003	5036
eCTP	2008Q3	61,978	15,543	1.62 (1.56–1.69)	1.49 (1.47–1.50)	0.697 ± 0.003	6226
MELD	2008Q3	61,978	15,543	1.10 (1.09–1.12)	1.09 (1.08–1.09)	0.648 ± 0.003	3211
VACS ^b	2008Q3	61,978	15,543	1.45 (1.40–1.49)	1.32 (1.31–1.33)	0.671 ± 0.003	5257

^aFine and Gray likelihood ratio test.

^bPer 10-unit change in regressor.

Supplementary Table 6. Performance of eCTP, MELD, and VACS in Predicting 5-year TFS in Specific Patient Subgroups

Subgroup	N	Median eCTP	Median MELD	Median VACS	Actual TFS	Predicted survival		
						eCTP ^a	MELD ^a	VACS4 ^{a,b}
Severe ascites	564	10	16	61	190 (152–243)	444 (384–487)	1256 (1157–1344)	1031 (985–1092)
Severe encephalopathy	938	10	15	59	297 (246–338)	444 (384–487)	1462 (1368–1558)	1205 (1100–1289)
Total bilirubin > 3	2470	9	18	52	485 (447–524)	653 (613–715)	861 (768–934)	1407 (1332–1470)
Creatinine > 3	555	7	28	81	712 (549–815)	1548 (1486–1606)	534 (358–797)	626 (535–732)
INR > 2.3	825	9	23	56	963 (885–1088)	653 (613–715)	633 (462–835)	1205 (1100–1289)
Coumadin exposed	1106	7	18	48	1452 (1311–1589)	1548 (1486–1606)	861 (768–934)	1690 (1572–1763)

^aNot adjusted for age and gender.^bVACS score binned by 5 (0–4, 5–9, 10–14, etc).1688
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