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Original Article

In-hospital outcomes of percutaneous ablative therapy for colorectal cancer liver metastasis in patients with and without frailty: nationwide inpatient sample analysis 2005-2020

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Abstract: Percutaneous ablative therapies are widely used to treat colorectal liver metastases (CRLM), particularly in patients who are not candidates for surgical resection. Frailty has been associated with poor outcomes in colorectal cancer (CRC) and liver resections. This study aimed to evaluate the clinical impact of frailty on short-term outcomes in patients undergoing percutaneous ablative therapies for CRLM. This population-based, retrospective study used data from the US Nationwide Inpatient Sample database (2005-2020). Adults aged ≥ 50 years diagnosed with CRLM who underwent percutaneous ablative therapies were included. Frailty was confirmed using the Hospital Frailty Risk Score (HFRS). Associations between frailty and in-hospital mortality, length of hospital stay (LOS), non-home discharge, total hospital charges, and postoperative complications were evaluated using univariate and multivariable regression analyses. A total of 670 patients (mean age: 66.3 years) were included, of whom 23% were categorized as frail (HFRS ≥ 5). Multivariable analysis showed that frail patients had significantly increased risks of complications (adjusted odds ratio [aOR] = 4.80, 95% confidence interval [CI]: 3.04-7.59), longer LOS (adjusted Beta [aBeta] = 1.69 days, 95% CI: 1.68-1.70), and higher total hospital charges (aBeta = $22.04 thousand, 95% CI: $21.92-$22.16). Complications with the highest risks in frail patients included, sepsis/shock (aOR = 17.39), surgical site infection (aOR = 3.55), respiratory failure/mechanical ventilation (aOR = 4.43), acute kidney injury (aOR = 9.37), and bleeding (aOR = 4.79). In conclusion, in adults aged ≥ 50 years undergoing percutaneous ablative therapies for CRLM, frailty independently predicted worse short-term outcomes, including higher complication rates, longer LOS, and increased hospital charges. The absence of detailed tumor characteristics and specific types of ablative therapy performed underscores the need for further research.

Keywords: Frailty, colorectal cancer, colorectal cancer liver metastasis, percutaneous ablation, radiofrequency ablation, in-hospital outcome

Introduction

In the United States (US), colorectal cancer (CRC) is the third most diagnosed cancer and the third leading cause of cancer-related death [1]. At diagnosis, 20% of CRC patients have distant metastasis, with the liver as the most common site due to the substantial intestinal mesenteric drainage into the hepatic portal venous system [2]. Management of colorectal liver metastases (CRLM) has evolved to prioritize personalized care, incorporating a range of treatment modalities such as surgical resection, local ablative therapies, and palliative interventions [3].

With respect to CRLM that is unresectable, percutaneous ablative therapies have been shown to improve overall survival (OS) and is a key treatment option [4]. These therapies utilize different mechanisms for controlled tissue ablation: radiofrequency ablation (RFA) and microwave ablation generate thermal energy, while cryoablation employs extreme cold. Among

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these, percutaneous RFA stands out as a minimally invasive technique in which radiofrequency energy is delivered directly to the target tissue through a needle-like electrode inserted through the skin. Guided by imaging modalities such as ultrasound, CT, or MRI, percutaneous RFA is frequently employed in oncology for tumor treatment, particularly in cases where surgical options are not viable [5]. Local tumor control rates for CRLM achieved with RFA have been reported to range between 47% and 96% [6, 7]. Although effective for treating CRLM, percutaneous ablative therapies have notable limitations. These include being time-intensive, presenting technical challenges when performed near large blood vessels due to heat-sink effects, and exhibiting a significant local failure rate of 20% to 40% [8].

The mainstream view defines frailty as a decline in physical functions or as the accumulation of multiple health deficits such as chronic diseases, physical function, sensory function, mental health, cognitive function [8, 9]. Further, frailty status is considered an effective measure for risk assessment, and is recognized as a favorable predictor of poor surgical outcomes [10]. In patients with CRC, frailty is associated with worse OS, cancer-specific survival (CSS), and recurrence-free survival (RFS) [11]. Besides, frailty is a known factor in predicting postoperative complications in older patients undergoing colon or rectal resection, as well as liver resection [12-14]. However, its impact on outcomes in patients undergoing minimally invasive, non-surgical procedures like percutaneous ablative therapy remains unclear. This represents a critical gap in the current understanding of how frailty affects the management and outcomes of CRC patients.

Given the significant burdens that frailty and CRC impose on the healthcare system, coupled with the scarcity of studies assessing the impact of frailty on the outcomes of percutaneous ablative therapies for CRLM - therapies often regarded as less invasive with fewer complications - it is crucial to explore this area further. The aim of this study was to evaluate the relations between frailty and short-term outcomes in patients undergoing percutaneous ablative therapy for CRLM. The analysis utilized a large, nationally representative dataset from the US.

Methods

Study design and database

This population-based, retrospective observational study used data from the US Nationwide Inpatient Sample (NIS) database. The NIS is the largest, comprehensive inpatient care database in the US, covering around 8 million hospital admissions annually and compiling data from all payer sources [15]. The Healthcare Cost and Utilization Project (HCUP), a division of the US National Institutes of Health (NIH), manages the NIS database. The NIS contains patient information such as primary and secondary diagnoses, primary and secondary procedures, admission and discharge status, patient demographic information, anticipated payment source, length of hospitalization, and hospital attributes such as bed capacity, location, teaching status, and geographical region. The continuously updated NIS database draws patient data from approximately 1,050 hospitals located in 44 states in the US. As classified by the American Hospital Association, the NIS database constitutes a 20% stratified sample of US community hospitals.

Ethics statement

All data used in this study were obtained through a formal request to the Online HCUP Central Distributor, which holds administrative responsibility for the database under certificate number HCUP-1I82IWT18. This study strictly adheres to the data-use agreement established with HCUP for utilizing the NIS database.

As this research relies on the analysis of secondary data derived from the NIS database, there was no direct involvement of patients and the public. The study protocol was reviewed by the Institutional Review Board (IRB) of Wan Fang Hospital, which granted an exemption from requiring formal IRB approval. Furthermore, given that all data within the NIS database are anonymized and devoid of personal identifiers, the need for informed consent was also waived as per established ethical guidelines.

Patient inclusion and exclusion

The NIS database was screened for adults ≥ 50 years old admitted to US hospitals with a diag-

nosis of CRC and metastasis to the liver, who underwent percutaneous ablative therapy (including RFA, microwave, or other thermal techniques) for the treatment of liver metastasis during 2005 and 2020. Diagnoses and surgical procedures were identified using the International Classification of Diseases, Ninth Revision (ICD-9) and Tenth (ICD-10) revision diagnostic and procedure codes, as detailed in Supplementary Table 1. Patients with incomplete data of sex, in-hospital outcomes, lacking sample weight values, or received surgical resection of the liver were excluded (Supplementary Table 1). The included patients were further categorized into frail and non-frail groups based on the criteria described below.

Study outcomes

The study outcomes were: 1) in-hospital mortality; 2) length of hospital stays (LOS); 3) non-home discharge; 4) total hospital charges; and 5) postoperative complications. Complications examined included: venous thromboembolism (VTE), pneumonia, sepsis/shock, surgical site infection/wound complication, respiratory failure/mechanical ventilation, acute kidney injury (AKI), urinary tract infection (UTI), bleeding, and digestive system complications, identified through the corresponding ICD-9 and ICD-10 codes listed in Supplementary Table 1.

Assessment of frailty

Frailty status was confirmed using the Hospital Frailty Risk Score (HFRS), a novel measure derived from an extensive range of ICD diagnostic codes employed as proxies for frailty-related conditions, with increasing utilizations. These codes encompass conditions such as volume depletion, chronic pulmonary disease, and heart failure and the HFRS has been validated [16]. In this analysis, patients with an HFRS score of 5 or higher were categorized as frail, while those with an HFRS score below 5 were classified as non-frail, in accordance with previous research [17].

Covariates

Data considered covariates extracted from the NIS included age, sex, race/ethnicity, insurance status and payer, and smoking status. Additional data extracted included emergent admission, comorbidities, and hospital-related characteristics such as bed capacity, weekend admission, annual procedure load of percutaneous ablation, location/teaching status, and hospital region. Comorbidities considered included: obesity, diabetes mellitus (DM), chronic pulmonary disease, chronic kidney disease (CKD), hypothyroidism, alcohol abuse, non-alcoholic fatty liver disease (NAFLD), and liver cirrhosis, identified through relevant ICD codes (Supplementary Table 1). Charlson Comorbidity Index (CCI) were used to represent the overall comorbidity burden of a patient.

Statistical analysis

Descriptive statistics were used to summarize patient demographics and clinical characteristics, with categorical variables presented as counts and weighted percentages and continuous variables as means with standard errors (SE). Group comparisons for categorical variables were conducted using the Rao-Scott chi-square test, while weighted mean differences for continuous variables were analyzed using survey methods that account for stratification, clustering, and sampling weights, ensuring valid and robust statistical inferences within the context of complex survey designs. Linear regression analysis was carried out to estimate coefficients (Beta) and corresponding 95% confidence intervals (CIs) for continuous outcomes, while logistic regression analysis was used to calculate odds ratios (ORs) and 95% CIs for binary outcomes, adjusting for relevant covariates. A two-sided p-value of < 0.05 was considered statistically significant. All analyses accounted for the NIS's complex survey design to ensure accurate national estimates. Statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Patient selection

The flow diagram of patient selection process is depicted in **Figure 1**. A total of 784 adults aged over 50 years, diagnosed with CRLM, and underwent percutaneous liver ablation, were included from the 2005-2020 NIS database. After applying the exclusion criteria, finally, 670 patients were included in the analyses, consisting of 157 patients who were classified as frail and 513 cases non-frail. This sample repre-

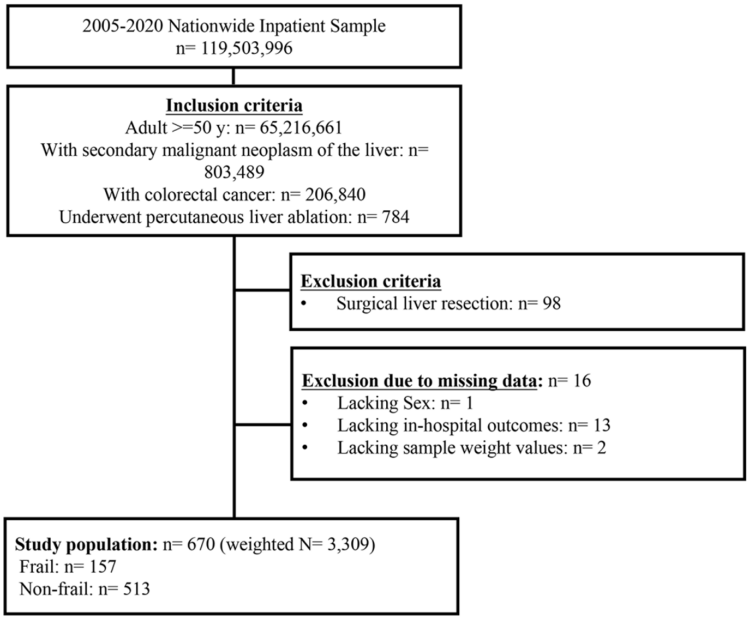

Figure 1. Flow diagram of patient selection and inclusion.

sents a total of 3,309 hospitalizations in the entire US after proper weighting.

Characteristics of the study population

Statistics of demographics, hospital-related information, and comorbidities of the study population are summarized in **Table 1**. The mean age of all patients was 66.3 years. 56.6% were male, 78.0% were white, and 58.5% had insurance covered by Medicare/Medicaid. The most common comorbidity was DM (24.1%). Significant differences between the 2 groups were observed in age, smoking status, study (admission) year, and admission type, as well as several comorbidities, CCI, hospital bed capacity, and hospital location/teaching status (**Table 1**).

The statistics of study outcomes categorized by frailty status are summarized in **Table 2**. The proportions of any complication, pneumonia, sepsis/shock, surgical site infection/wound complication, UTI, respiratory failure/mechanical ventilation, AKI, and bleeding were significantly higher in patients with frailty compared to those without frailty (all *p*-values < 0.001). LOS was longer in patients with frailty than in those without frailty (mean: 4.9 vs. 2.8 days, P = 0.005). Additionally, a higher proportion of non-home discharges was observed in patients with frailty compared to those without frailty (6.7% vs. 3.6%, P = 0.031) (**Table 2**).

Associations between frailty and outcomes

Associations of frailty status and study outcomes in the study population are summarized in **Table 3**. After adjusting for relevant confounders in the multivariable analysis, we found that patients with frailty had significantly longer LOS (adjusted Beta [aBeta] = 1.69, 95% CI: 1.68-1.70, P < 0.001) and greater total hospital charges (aBeta = 22.04, 95% CI: 21.92-22.16, P < 0.001) compared to those without frailty. Patients with frailty were found to have significantly higher risks of complications (adjusted OR [aOR] = 4.80, 95% CI: 3.04-7.59, P < 0.001) than those without frailty (**Table 3**).

Associations between frailty and individual complications

Further analyses were conducted to explore the associations between frailty status and detailed complications, and the results are summarized in **Figure 2**. Patients with frailty had significantly higher risks of sepsis/shock (aOR = 17.39, 95% CI = 6.84, 44.21), surgical site infection/wound complication (aOR = 3.55, 95% CI = 1.46, 8.63), respiratory failure/mechanical ventilation (aOR = 4.43, 95% CI = 1.93, 10.20), AKI (aOR = 9.37, 95% CI = 3.56, 24.68), and bleeding (aOR = 4.79, 95% CI = 2.35, 9.78) (all *p*-values < 0.005). (**Figure 2**).

Discussion

In this study of adults aged 50 years and older in the US who underwent percutaneous ablative therapies for CRLM, approximately 23% of patients were identified as frail based on the HFRS. Frailty was independently associated with worse in-hospital outcomes, including significantly longer hospital stays (mean increase of 1.7 days), higher total hospital charges, and a 4.8-fold increased risk of complications compared to non-frail patients. Specific complica-

Table 1. Characteristics of the study population, categorized by frailty status

Characteristics	All (n = 670)	Non-frail (n = 513)	Frail (n = 157)	*p-value*
Age, years	66.3 ± 0.3	65.9 ± 0.4	67.8 ± 0.6	**0.041**
50-59	185 (27.7)	149 (29.2)	36 (22.5)	0.129
60-69	243 (36.5)	186 (36.5)	57 (36.5)	
70-79	170 (25.1)	127 (24.4)	43 (27.6)	
≥ 80	72 (10.7)	51 (9.9)	21 (13.4)	
Sex				0.936
Male	380 (56.6)	290 (56.6)	90 (56.9)	
Female	290 (43.4)	223 (43.4)	67 (43.1)	
Race/ethnicity				0.457
White	494 (78.0)	380 (78.1)	114 (77.6)	
Black	49 (7.8)	35 (7.3)	14 (9.4)	
Hispanic	50 (7.9)	38 (7.8)	12 (8.4)	
Others	40 (6.3)	33 (6.8)	7 (4.6)	
Missing	37	27	10	
Smoking	194 (29.0)	137 (26.9)	57 (36.0)	**0.007**
Insurance status/primary payer				0.632
Medicare/Medicaid	392 (58.5)	296 (57.7)	96 (61.3)	
Private including HMO	255 (38.2)	198 (38.8)	57 (36.1)	
Self-pay/no-charge/other	22 (3.3)	18 (3.5)	4 (2.6)	
Missing	1	1	0	
Study year				**< 0.001**
2005-2010	217 (31.9)	157 (30.2)	60 (37.6)	
2011-2015	144 (21.4)	83 (16.0)	61 (39.1)	
2016-2020	309 (46.7)	273 (53.8)	36 (23.3)	
Emergent admission	108 (16.1)	71 (13.8)	37 (23.5)	**< 0.001**
Missing	4	4	0	
Comorbidities				
Obesity	69 (10.4)	39 (7.7)	30 (19.3)	**< 0.001**
DM	162 (24.1)	117 (22.7)	45 (28.7)	0.093
Chronic pulmonary disease	90 (13.4)	62 (12.1)	28 (17.9)	**0.023**
CKD	45 (6.8)	19 (3.7)	26 (16.9)	**< 0.001**
Hypothyroidism	45 (6.7)	30 (5.8)	15 (9.5)	**0.033**
Alcohol abuse	6 (0.9)	5 (1.0)	1 (0.6)	0.294
NAFLD	17 (2.6)	11 (2.2)	6 (3.8)	0.173
Liver cirrhosis	14 (2.1)	12 (2.3)	2 (1.3)	0.254
CCI				**< 0.001**
0	374 (56.0)	308 (60.1)	66 (42.3)	
1	173 (25.7)	135 (26.2)	38 (23.8)	
2	71 (10.5)	47 (9.1)	24 (15.2)	
3+	52 (7.8)	23 (4.5)	29 (18.7)	
Annual procedure volume				0.386
Low	198 (29.5)	155 (30.1)	43 (27.4)	
High	472 (70.5)	358 (69.9)	114 (72.6)	
Weekend admission	14 (2.1)	6 (1.2)	8 (5.1)	**< 0.001**
Hospital bed capacity				**0.025**
Large (> 450)	512 (76.8)	390 (76.4)	122 (78.3)	
Medium (250-450)	112 (16.8)	91 (17.7)	21 (13.8)	
Small (< 250)	45 (6.4)	32 (5.9)	13 (7.9)	
Missing	1	0	1	

Hospital location/teaching status				**0.028**
Urban teaching	566 (84.7)	439 (85.6)	127 (81.8)	
Urban nonteaching	96 (14.3)	70 (13.7)	26 (16.4)	
Rural	7 (1.0)	4 (0.8)	3 (1.8)	
Missing	1	0	1	
Hospital region				0.622
Northeast	172 (26.1)	135 (26.6)	37 (24.4)	
Midwest	125 (18.7)	95 (18.6)	30 (19.0)	
South	252 (37.3)	195 (37.8)	57 (36.0)	
West	121 (17.9)	88 (17.0)	33 (20.7)	

Abbreviations: DM, diabetes mellitus; CKD, chronic kidney disease; NAFLD, non-alcoholic fatty liver disease; HMO, Health Maintenance Organization; CCI, Charlson's Comorbidity Index. Continuous variables are presented as mean ± SE; categorical variables are presented as unweighted counts (weighted percentage). *P*-values < 0.05 are shown in bold.

Table 2. Outcomes of the study population, categorized by frailty status

Outcomes	All (n = 670)	Non-frail (n = 513)	Frail (n = 157)	*p-value*
Complication, any	148 (22.2)	88 (17.2)	60 (38.6)	**< 0.001**
VTE	11 (1.7)	7 (1.4)	4 (2.6)	0.240
Pneumonia	11 (1.7)	2 (0.4)	9 (5.8)	**< 0.001**
Sepsis/shock	27 (4.1)	8 (1.6)	19 (12.4)	**< 0.001**
Surgical site infection/wound complication	20 (3.0)	9 (1.7)	11 (7.0)	**< 0.001**
UTI	18 (2.7)	9 (1.8)	9 (5.9)	**< 0.001**
Respiratory failure/mechanical ventilation	22 (3.3)	12 (2.3)	10 (6.5)	**< 0.001**
AKI	31 (4.7)	11 (2.1)	20 (12.9)	**< 0.001**
Bleeding	34 (5.1)	13 (2.5)	21 (13.5)	**< 0.001**
Digestive system complication	58 (8.7)	43 (8.4)	15 (9.8)	0.535
In-hospital mortality	1 (0.2)	0 (0.0)	1 (0.7)	-
LOS, days[a]	3.3 ± 0.2	2.8 ± 0.1	4.9 ± 0.7	**0.005**
Non-home discharge[a]	28 (4.3)	18 (3.6)	10 (6.7)	**0.031**
Total hospital charges, per 1,000 dollars	65.5 ± 3.1	62.7 ± 2.8	74.7 ± 8.0	0.198

Abbreviations: VTE, venous thromboembolism; LOS, length of stays; AKI, acute kidney injury; UTI, urinary tract infection. Continuous variables are presented as mean ± SE; categorical variables are presented as unweighted counts (weighted percentage). [a]Excluding patients who died in hospitals. *P*-values < 0.05 are shown in bold.

Table 3. Associations between frailty and outcomes

Outcomes	Comparison	aBeta/aOR (95% CI)	*p-value*
Non-home discharge[a,b]	frail vs. non-frail	0.65 (0.36-1.19)	0.160
LOS, days[a,c]	frail vs. non-frail	1.69 (1.68-1.70)	**< 0.001**
Total hospital charges[d]	frail vs. non-frail	22.04 (21.92-22.16)	**< 0.001**
Complication, any[e]	frail vs. non-frail	4.80 (3.04-7.59)	**< 0.001**

Abbreviations: OR, odds ratio; CI, confidence interval; LOS, length of stay. [a]Excluding patients who died in hospitals. [b]Adjusted for significant variables in the univariate analysis including sex, race/ethnicity, insurance status, chronic pulmonary disease, CKD, hypothyroidism, CCI, weekend admission, hospital bed capacity, and location/teaching status. [c]Adjusted for significant variables in the univariate analysis including race/ethnicity, study year, emergent admission, chronic pulmonary disease, CKD, CCI, and hospital region. [d]Adjusted for significant variables in the univariate analysis including race/ethnicity, study year, emergent admission, obesity, CKD, CCI, and hospital region. [e]Adjusted for significant variables in the univariate analysis including race/ethnicity, smoking status, study year, emergent admission, obesity, chronic pulmonary disease, CKD, hypothyroidism liver cirrhosis, annual procedure volume levels, weekend admission, and hospital location/teaching status. *P*-values < 0.05 are shown in bold. aBeta for continuous outcomes (LOS and total hospital charges), while aOR for binary outcomes (non-home discharge and any complication).

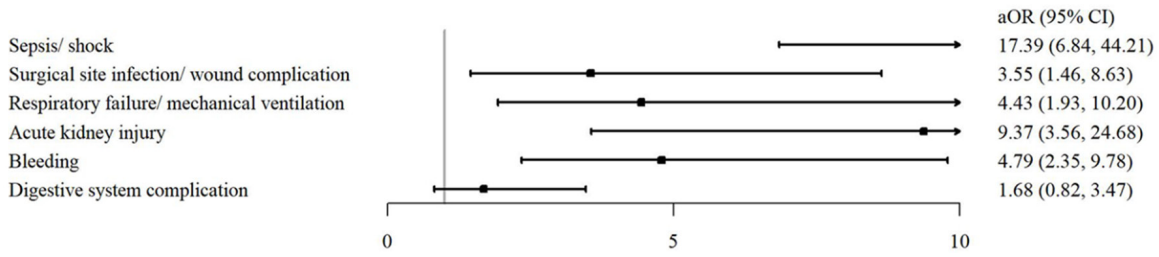

Figure 2. Associations between frailty status and individual complications. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval. Adjusted for significant variables in the univariate analysis (except for no event occurred) including race/ethnicity, smoking status, study year, emergent admission, obesity, chronic pulmonary disease, CKD, hypothyroidism, liver cirrhosis, annual procedure volume, weekend admission, and hospital location/teaching status.

tions strongly impacted by frailty are sepsis/shock, surgical site infection/wound complication, respiratory failure/mechanical ventilation, AKI, and bleeding. These findings underscore the substantial influence of frailty on short-term outcomes, even in the context of minimally invasive therapies like percutaneous ablation, highlighting that frailty is a critical determinant of perioperative risk. This suggests that clinicians should carefully weigh frailty status when considering percutaneous ablative therapies as an option for managing CRLM.

Frailty's influence in the context of percutaneous ablative therapies for CRLM specifically has seldom been evaluated. Therefore, direct comparisons between our findings and prior research may not be applicable. However, numerous studies in the literature have examined the impact of frailty on CRC outcomes, as well as on the outcomes of surgically treated CRLM [13, 18-24]. For example, Tokuda et al. [13] studied patients who underwent hepatectomy for CRLM, where frail was defined based on a score of ≥ 4 on a clinical frailty scale. Frailty was consistently shown to be an independent and strong unfavorable prognostic factor in such settings.

It should be noted that, among the various frailty assessment tools, the HFRS was chosen for this study due to its validated use in large administrative databases and its reliance on ICD-coded comorbidities. Compared to the Clinical Frailty Scale (CFS), Fried Frailty Phenotype, and Modified Frailty Index (mFI), which incorporate functional and physiological parameters, HFRS enables standardized frailty assessment in retrospective studies utilizing inpatient datasets. Moreover, while HFRS is typically applied to older populations (≥ 65 or ≥ 75 years), studies have also validated its use in younger adults. Kumar et al. found that nearly two-thirds of frail hospitalized patients with chronic pancreatitis were under 65, while Kutrani et al. demonstrated that HFRS effectively predicts hospital length of stay across all adult age groups [25, 26]. Consequently, our study included population younger than 65 years for a more comprehensive assessment. While prior studies have demonstrated that HFRS correlates well with other frailty indices in predicting perioperative risk or hospitalization outcomes [27, 28], its predictive performance in minimally invasive oncologic procedures such as percutaneous ablation remains an area for further investigation.

Similarly, Dauch et al. [20] identified 5,230 patients who received liver resection for CRLM in a surgical quality improvement database, and classified patients into 3 groups using the 5-item Modified Frailty Index. Patients with a score ≥ 2 were significantly more likely to have minor and major complications, readmission, unfavorable discharge, 30-day mortality, prolonged LOS, and bile leakage. A recent study used the NIS to identify older patients who received a hepatic resection under various indications from 2012 to 2019, and defined frailty using a Johns Hopkins frailty indicator [21]. Frailty was associated with a significantly increased risks of mortality and complications, as well as increased LOS and hospital costs. Our findings align with these observations, as frail patients in our cohort similarly experienced prolonged hospital stays and higher complication risks. Shahrestani et al. [24] identified patients who underwent resection of a secondary neoplasm of the liver from 2016 to

2017 in the Nationwide Readmissions Database. Frailty, defined using the Johns Hopkins frailty indicator, was associated with significantly higher rates of nonroutine discharge, longer LOS, and greater cost as well as a higher mortality rate. Additionally, Mima et al. [23] studied patients receiving hepatectomy for CRLM between 2004 and 2020 which utilized the Clinical Frailty Scale to define frailty. It showed that frailty was an independent factor of worse OS, DFS, and CSS. These results parallel our findings and reinforce the notion that frailty independently predicts adverse outcomes, regardless of whether the treatment modality is surgical or minimally invasive procedures like percutaneous ablations. Future studies comparing different frailty measures in this specific context may further help refine risk stratification and optimize patient selection.

Though not specifically examining for patients with frailty, studies of RFA for the treatment of CRLM and liver tumors have generally shown good short-term outcomes [29-32]. Shullian et al. [30] reported the results of 1,235 multiprobe stereotactic RFA sessions for liver tumors for 793 consecutive patients with a median age of 65 years. The 30-day mortality was 0.5%, and the overall major complication rate decrease from 11% to 6% as more procedures were performed. Factors associated with major complications (i.e., hemorrhage, pneumothorax) included history of bile duct surgery, tumors in segment IVa or VIII, and the number of coaxial needles used. Akhan et al. [29] reported the results of patients who received RFA for CRLM. No major complications were reported, and the minor complication rate was 7%. The 1-, 3-, and 5-year OS rates were 94.9%, 52.5%, and 40.6%, respectively. The 1-, 3-, and 5-year DFS rates were 44%, 10.2%, and 6.7%, respectively. The median survival was 25 months in patients with metastasis size of > 3 cm, while it was 42 months in patients with metastasis size of ≤ 3 cm (P = 0.001). Multiple metastasis was associated with worse OS and DFS. A systematic review and meta-analysis by Yang et al. [32] compared RFA and hepatic resection for treatment of CRLM. Twenty-two studies with approximately 4,400 patients were included in the analysis. The 30-day mortality rate was similar between resection and RFA, but RFA was associated with a higher recurrence rate and poorer long-term survival. Besides, an international, multicenter, phase III randomized controlled trial revealed transitioning to thermal ablation as the standard treatment for small CRLM (≤ 3 cm) may reduce complications and hospital stays while enhancing local control, without impacting disease-free or overall survival [33]. Further research is warranted to investigate these downstream effects, as long-term outcomes were beyond the scope of our study.

Several studies investigated RFA alongside other treatments. Wang et al. [34] observed 81 patients with unresectable CRLM treated with RFA, noting minimal complications and a median local tumor progression-free survival (PFS) of 30 months. Lesion size (> 3 cm) and early local tumor progression correlated with shorter survival, while post-RFA chemotherapy showed improved prognosis. Fu et al. [35] compared CRC resection with RFA of CRLM against CRC resection with resection of CRLM in groups of 53 patients each. Combined CRC resection and RFA resulted in reduced intraoperative blood loss, shorter hospital stays, and comparable long-term survival but higher tumor recurrence rates. Chen et al. [36] compared NAC + RFA versus NAC + liver resection for CRLM, finding similar 1- and 3-year overall survival rates (74%). However, the liver resection group showed lower 1- and 3-year progression-free survival rates compared to the RFA group.

Overall, our study adds to the growing body of evidence on frailty in oncology by uniquely focusing on minimally invasive percutaneous therapies for CRLM. While RFA and similar procedures are often perceived as less invasive alternatives to surgery, our findings indicate that frailty remains a significant barrier to achieving optimal outcomes. This highlights the importance of incorporating frailty assessments into preprocedural planning and exploring targeted interventions to improve resilience and reduce risk in this vulnerable population.

Strength and limitations

This study is the first to examine the prognostic impact of frailty on short-term outcomes following percutaneous ablative therapy for CRLM. One notable strength of this research is its extensive dataset, enabling the analysis of diverse complications in a representative sample of the nationwide population. However, several limitations should be recognized. First, the ret-

rospective design of this analysis carries a lower level of evidence compared to a prospective study. Second, the accuracy of diagnosis and procedures in this study heavily depended on ICD codes, which may not precisely capture clinical conditions or procedures. Importantly, the ICD codes used in the analysis cannot distinguish between specific types of percutaneous ablations, such as microwave ablation or cryoablation, requiring these procedures to be analyzed collectively. This is a potential limitation, as these techniques may differ in their efficacy and complication profiles. Third, the NIS lacks temporal data to distinguish synchronous from metachronous liver metastases, which may impact treatment strategies and outcomes. Furthermore, the study lacked detailed information about patient preoperative performance status, as well as intraoperative parameters. Also, most importantly, the exact size, anatomic location, and number of tumors in the liver was not reported, and thus could not be included in the analysis. The NIS is a claims-based database that primarily captures procedures related to the current hospitalization. As a result, prior chemotherapy and radiotherapy may not be coded and therefore could not be included in the analysis. This limitation highlights the need for further investigation using datasets with more comprehensive longitudinal treatment records. The last significant limitation is the lack of follow-up data after discharge, thereby analysis on the long-term prognostic impact of frailty after discharge could not be done.

Conclusions

This study is the first to assess the prognostic impact of frailty on short-term outcomes following percutaneous ablative therapies for CRLM in a nationally representative cohort. Our analysis indicates that frailty is independently associated with worse in-hospital outcomes, including prolonged hospital stays, higher complication rates, and increased hospital charges. However, the absence of detailed tumor characteristics and the specific types of ablative therapy performed highlights the need for further research. Future studies should aim to validate these findings, explore the long-term implications of frailty in this population, and investigate strategies to optimize outcomes, including personalized interventions and refined patient selection criteria.

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Disclosure of conflict of interest

None.

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Supplementary Table 1. ICD codes used in the study

Condition	ICD-9 code	ICD-10 code
Secondary malignant neoplasm of the liver	CM: 197.7	CM: C78.7
Colorectal cancer	CM: 153, 154.0, 154.1, V10.05, V10.06	CM: C18-20, Z85.03, Z85.04
Percutaneous ablation of the liver	PCS: 50.24	PCS: 0F503, 0F504, 0F513, 0F514, 0F523, 0F524
Surgical resection of the liver	PCS: 50.21, 50.22, 50.3, 50.4, 50.5	PCS: 0FB00ZZ, 0FB03ZZ, 0FB04ZZ, 0FB13ZZ, 0FB14ZZ, 0FB15ZZ, 0FB23ZZ, 0FB24ZZ, 0FB25ZZ
VTE	CM: 415, 451-453, 671, 673, 997.2	CM: I260, I269, I801-803, I808, I809, I820-I823, I828, I829, 0082, 0223, 0871, 0882, I81, I82
Sepsis	CM: 995.9, 996.64, 038, 999.3, 790.7, 041, 785.52	CM: R78.81, A41, R65.2, T81.4, T80.2, A42.7, A22.7, B37.7, A26.7, A28.2, A54.86, B00.7, A32.7, A24.1, A39.2, A20.7, A21.7, A48.3
Surgical site infection/Wound complication	CM: 998.59, 998.51, 998.3, 998.83, 998.0, 998.31, 998.32, 998.33, 998.12-998.13, 998.5	CM: T81.4XXA, T81.4XXD, T81.4XXS, 086.0, 086.1, T81.3
Urinary tract infection	CM: 590.1, 590.2, 590.3, 595.0, 599.0, 599.1	CM: N39.0, N30.00, N30.01, N30.10, N30.11, N30.20, N30.21, N30.22, N30.9, N39.1, N39.3, N39.4, N10, N11, N12, N13
Respiratory failure	CM: 518.5, 518.81-518.84	CM: J95.2-J95.8, J96.00, J96.90, J80, J81.0
Mechanical ventilation	PCS: 96.7	PCS: 5A1935Z, 5A1945Z, 5A1955Z
AKI	CM: 584 DXCCS: 157	CM: N17 DXCCSR_GEN002 >0
Shock	CM: 998.0, 785.5, 995.4	R57, T81.1, T88.2, R65.21
Bleeding	CM: 998.1, 998.2, 998.51, 285.1 PCS: 99.0	CM: G05.3, G05.4, G08, G43, G44, G50-G59, G60.3, G61.0, G61.81, G61.82, G61.9, G62.81, G63, G70.1, G70.9, G73.3, M79.1, M79.2
Wound complication	CM: 998.3, 998.83, 998.0, 998.31, 998.32, 998.33, 998.12-998.13, 998.5	CM: T81.3
Digestive system complication	CM: 997.4, 998.59, 567.22	CM: K66.0, K65.1, K68.11, K91.8
Smoking	CM: 305.1, V15.82, 989.84	CM: Z71.6, Z72.0, Z86.43, Z87.891, F17, O99.33, T65.2
Obesity	CM: 278.00, 278.01, 278.03, V85.3-V85.4 DXCCS: CM_OBESE	CM: E66.0-E66.2, E66.8, E66.9, Z68.3-Z68.4 DXCCSR_END009
DM	CM: 250 DXCCS: CM_DM	CM: E10-E13
Chronic pulmonary disease	CM: 416.8, 416.9, 490-505, 506.4, 508.1 DXCCS: CM_CHRNLUNG	CM: I27.8, I27.9, J40-J47, J4A, J68.4, J70.1, J70.3
CKD	CM: 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582, 583.0-583.7, 585, 586, 588.0, V42.0, V45.1, V56	CM: I12.0, I13.1, N03.2-N03.7, N05.2-N05.7, N18, N19, N25.0, Z49.0, Z49.2, Z94.0, Z99.2
Hypothyroidism	CM: 243, 244	CM: E02, E03
Alcohol abuse	CM: 303, 305.0, 571.0, 571.3	CM: F10, K70.0, K70.9
NAFLD	CM: 571.8, 571.9	CM: K76.0, K75.8, K73
Liver cirrhosis	CM: 571.2, 571.5, 571.6	CM: K74.1-K74.6

Abbreviations: AKI, acute kidney injury; CM, clinical modification; ICD, International Classification of Disease; DM, diabetes mellitus; PCS, procedures; VTE, venous thromboembolism; CKD, chronic kidney disease; NAFLD, non-alcoholic fatty liver disease.