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Liver resection versus ablation in geriatric populations - Does one method impart improved in-hospital mortality?

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ABSTRACT

Objective: This study aimed to compare surgical resection versus ablation for managing liver malignancies in patients 65 and older.

Material and Methods: Cases with liver tumors were extracted from the NSQIP database for patients aged ≥65 years. Following propensity score matching, multivariate Cox regression was used for 30-day morbidity and mortality for liver resection and ablation.

Results: Following a propensity score matching, 1048 patients were 1:1 matched for comorbid conditions. Patients stayed in the hospital three days longer after resection (p< 0.001). Mortality was lower after ablation (p= 0.013). This difference was more prominent in patients with primary liver tumors (p= 0.008). Group A had a 10-fold lower risk of developing an abdominal abscess, a fourfold decrease in hospital-associated pneumonia (p= 0.001) and reintubation, a 10-fold reduction in bleeding requiring transfusion (p< 0.001), and a three-fold decrease in risk of developing sepsis (p< 0.001).

Conclusion: Despite being a generally sicker patient population with worse underlying liver function, ablative techniques were associated with a lower risk of adverse outcomes when compared to more aggressive resection of primary malignant tumors of the liver.

Keywords: Liver cancer, resection, ablation, complications

INTRODUCTION

There has been a marked increase in the percentage of the geriatric population in the United States. Over the next few decades, we expect nearly a quarter of the US population to be 65 years or older (1). Since this is the largest growing population subset, we must be equipped and ready to address the unique challenges the elderly population provides to the field of surgery. Physiologic reserve decreases with aging as the frailty level increases (2). There has been a significant concentration on preoperative optimization and "prehab" to address this need; however, little has been done to address different surgical options catering to the aging patient (3).

With the advancement in screening and imaging, there is an increasing number of patients with primary and secondary liver malignancies. With a higher number of liver tumors diagnosed, more patients require treatment. Under ideal circumstances, the treatment of choice for liver malignancies remains as resection (4). Most of the studies regarding liver ablation have been for secondary liver malignancies. Data demonstrate that overall survival is comparable. However, local recurrence rates are variable (5,6). Early complication rates in the literature are low for ablation (0-27%), with more recent literature citing the rate around 7% (7).

This study aimed to analyze the outcomes of liver resection and ablation for liver malignancies in patients aged 65 years or older. We hypothesized that elderly patients undergoing resection would have higher complication rates and 30-day mortality.

MATERIAL and METHODS

Data were obtained from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP). ACS NSQIP is a national database that provides preoperative risk factors, operative data, and 30-day outcomes.

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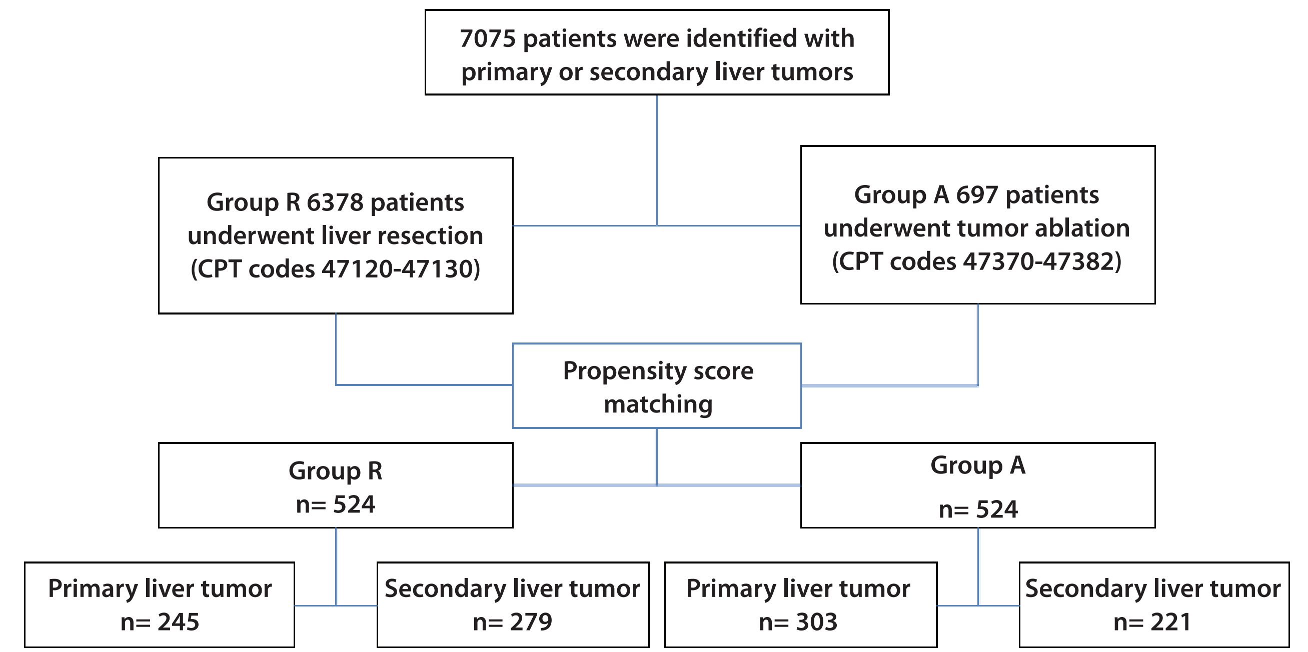

Figure 1. Flow diagram depicting the study cohorts.

The ACS NSQIP database was queried for patients aged 65 years and greater who had liver resection (Group R) or ablation (Group A) between 2008 and 2016 (Figure 1). These patients were identified using the International Classification of Diagnosis (ICD) and Current Procedural Terminology (CPT) codes (Group R: 47120-47130 and Group A: 47370-47382). Patients were excluded if there was missing information for diagnosis, length of stay, in-hospital, and 30-day mortality rates.

Data were collected for American Society of Anesthesiologists (ASA) classification, the number of units of packed red blood cells given intraoperatively, operating time (measured in minutes), length of hospital stay (measured in days), postoperative wound infection, organ space/surgical site infection, pulmonary complications, renal complications, cardiovascular complications, the frequency of returning to the operating room, readmission, 30-day, and in-hospital mortality rates. ASA classification is in accordance with the American Society of Anesthesiologists (8). Definitions of the data obtained are described in detail elsewhere (9).

Statistical Analysis and Data Management

Data were maintained on a spreadsheet (Excel, Microsoft®, Redmond, WA, USA) and analyzed using SPSS for Mac OS version 28.0 (IBM Inc. Chicago, IL). Mean data were presented with 95% confidence intervals where appropriate unless otherwise noted. We analyzed anthropometric and presurgical comorbid data and compared the two groups of patients based on their treatment modalities using Chi-square or Fisher's exact tests. We also utilized Chi-square tests to compare postoperative complications between the different interventions. The null hypotheses were rejected with a 95% confidence interval. Logistic regression models were also constructed to calculate the propensity scores. Data from groups R and A were matched by a 1:1 ratio using propensity score matching (PSM). We selected the variables based on their respective scores with a caliber of 0.1 decimal. The variables chosen for PSM included the chronic use of steroids, weight loss >10%, ascites, bleeding disorders and ASA physical status. Multivariate Cox proportional hazards regression was used for time-to-event analyses, and data are presented as odds/hazard ratio with confidence interval. A subgroup analysis was then carried out of primary versus secondary liver tumors (Figure 1).

RESULTS

Seven thousand seventy-five patients underwent surgical treatment for liver malignancy between 2008 and 2016, liver resection was performed in 6378 (Group R; 90%), and 697 (10%) underwent tumor ablation (Group A). Patient demographics were comparable between the two groups, apart from weight loss >10%, BMI, presence of ascites, bleeding disorders and prior use of corticosteroids (Table 1). One thousand forty-eight patients were included in the matched propensity analysis: 524 for each operative intervention modality. The prevalence of preoperative comorbid conditions was comparable between the two groups after the PSM. Preoperative comorbidities are also seen in Table 1 both before and after PSM.

Table 1. Patient demographics, clinical information, co-morbid diseases before and after propensity score matching. Asterisks indicate the variables included in propensity score matching

		Before Propensity Score Matching			After Propensity Score Matching		
Category		**Resection (n= 6378)**	**Ablation (n= 697)**	**P-value**	**Resection (n= 524)**	**Ablation (n= 524)**	**P-value**
Age (year)		72 ± 5	72 ± 5	0.437	72 ± 5	72 ± 6	0.068
Sex	Male	3744 (59%)	324 (61%)	0.270	302 (58%)	321 (61%)	0.257
	Female	2633 (41%)	205 (39%)		221 (42%)	202 (39%)	
Height (cm)		168 ± 10	168 ± 10	0.223	--	--	--
Weight (kg)		79 ± 18	81 ± 18	0.008	--	--	--
Body mass index		27.8 ± 5.6	28.3 ± 5.4	0.064	27.8 ± 5.7	28.3 ± 5.4	0.137
Caucasian race		4565 (72%)	398 (72%)	0.342	379 (72%)	364 (70%)	0.341
ASA II/III/IV*		953/4834/567	57/413/57	0.014	57/408/56	57/408/56	0.999
Diabetes mellitus		1599 (25%)	159 (25%)	0.999	159 (30%)	159 (30%)	0.999
COPD		348 (5.5%)	27 (5.1%)	0.842	39 (7.4%)	26 (5%)	0.842
Active smoking		685 (11%)	68 (13%)	0.147	57 (11%)	67 (13%)	0.398
Dyspnea		495 (7.8%)	50 (7.2%)	0.611	50 (9.5%)	36 (6.9%)	0.143
Dependent functional status		83 (1.3%)	7 (1.0%)	0.645	10 (1.9%)	6 (1.1%)	0.328
Ascites*		41 (0.6%)	22 (4.2%)	<0.001	24 (4.6%)	22 (4.2%)	0.786
Hypertension		4235 (66%)	343 (65%)	0.444	361 (69%)	338 (65%)	0.149
End-stage renal failure		17 (0.3%)	0 (0.0%)	0.636	--	--	--
Prior steroid use*		206 (3.2%)	26 (3.7%)	0.045	25 (4.8%)	25 (4.8%)	0.999
Weight loss >10%*		291 (4.6%)	14 (2.6%)	0.036	13 (2.5%)	13 (2.5%)	0.999
Bleeding disorder*		274 (4%)	69 (10%)	<0.001	57 (11%)	57 (11%)	0.999
Prior sepsis		439 (6.8%)	64 (9.2%)	<0.001	--	--	--

Table 2. Preoperative laboratory data (Mean ± Standard Deviation) before propensity score matching. These variables were not included in the matching, and they were fundamentally different between the two treatment modalities

Preoperative Labs	Resection (n= 524)	Ablation (n= 524)	P-value
Bilirubin (mg/dL)	0.74 ± 0.85	0.86 ± 0.64	0.009
Aspartate aminotransferase (unit/L)	37 ± 39	41 ± 32	0.003
Alkaline phosphatase (units/L)	114 ± 88	108 ± 57	0.016
Albumin (gram/dL)	3.9 ± 0.5	3.7 ± 0.6	<0.001
Hematocrit (percent)	38.6 ± 5.2	38.6 ± 4.9	0.771
White blood cells (counts/nL)	7.12 ± 3.34	5.73 ± 2.04	<0.001
Platelets (counts /nL)	218 ± 84	163 ± 74	<0.001
Prothrombin time (seconds)	12.3 ± 2.2	12.7 ± 2.1	0.173
International normalized ratio	1.05 ± 0.18	1.12 ± 0.22	<0.001
Sodium (mmol/L)	139.2 ± 3.1	138.8 ± 3.2	0.008
Creatinine (mg/dL)	0.98 ± 0.48	1.0 ± 0.56	0.390

In univariate analysis of the matched patients, preoperative laboratory data was notable for having higher bilirubin (0.86 ± 0.64 vs. 0.74 ± 0.85 mg/dL, p= 0.01), INR (1.12 ± 0.22 vs. 1.05 ± 0.18, p< 0.001), AST (41 ± 32 vs. 37 ± 39 units/L, p= 0.003) but lower platelets (163 ± 74 vs. 218 ± 84 counts/nL, p< 0.001) and albumin (3.7 ± 0.6 vs. 3.9 ± 0.5 gm/dL, p< 0.001) in Group A when compared to the patients in Group R (Table 2). Preoperative laboratory values were not included for PSM since these values were fundamentally different and any attempt to match for these variables revealed no matched subjects between groups R and A.

Table 3. The occurrence of postoperative complications in patients undergoing surgical resection versus ablation for liver tumors after propensity score matching in 1048 patients. The odds ratios were calculated based on the risk of a particular complication after liver ablation compared to liver resection

Preoperative Labs	Resection (R) (n= 524)	Ablation (A) (n= 524)	Odds Ratios 95% Confidence	P-value
Predicted risk of mortality (percent)	3.26 ± 3.67	1.64 ± 1.84	---	<0.001
Predicted risk of morbidity (percent)	23.7 ± 10.3	8.4 ± 5.8	---	<0.001
Operative duration of procedure (minutes)	226 ± 119	134 ± 82	---	<0.001
Total length of hospital stay (days)	7.9 ± 6.6	3.1 ± 4.5	---	<0.001
Any post-procedural morbidity	176 (33.6%)	38 (7.3%)	0.16 (0.11-0.23)	<0.001
Wound dehiscence/infection	22 (4.2%)	7 (1.3%)	0.31 (0.13-0.73)	0.007
Abdominal abscess formation	26 (5.0%)	3 (0.6%)	0.11 (0.03-0.37)	<0.001
Hospital-associated pneumonia	27 (5.2%)	7 (1.3%)	0.25 (0.11-0.58)	0.001
Re-insertion of endotracheal tube	17 (3.2%)	6 (1.1%)	0.35 (0.14-0.88)	0.033
Venous thromboembolism	14 (2.7%)	7 (1.3%)	0.49 (0.20-1.23)	0.130
Acute kidney injury	12 (2.3%)	5 (1.0%)	0.41 (0.14-1.18)	0.140
Urinary tract infections	16 (3.1%)	7 (1.3%)	0.43 (0.18-1.05)	0.090
Cerebrovascular event/stroke	4 (0.8%)	1 (0.2%)	0.25 (0.03-1.01)	0.374
Major adverse cardiac event	16 (3.1%)	3 (0.6%)	0.18 (0.05-0.63)	0.004
Major bleeding requiring transfusion	112 (21.4%)	14 (2.7%)	0.10 (0.06-0.18)	<0.001
Sepsis with or without shock	25 (4.9%)	7 (1.3%)	0.27 (0.12-0.63)	0.003
Death within 30 days	15 (2.9%)	5 (1.0%)	0.33 (0.12-0.91)	0.039

Postoperative Morbidities and Adverse Events

Postoperative occurrence of adverse events was analyzed in 1048 patients following PSM (Table 3). One hundred and seventy-six patients (33.6%) in Group R developed post-procedural complications, slightly higher than the risk of morbidity of 23.7 ± 10.3% predicted by the ACS risk calculator. In contrast, only 38 (7.3%) patients had reported post-procedural adverse events in Group A, which was on par with the 8.4 ± 5.8% risk calculated by ACS. Overall, there was a six-fold decrease in the risk of a postprocedural adverse event in Group A compared to group R [0.16 (0.11-0.23); p< 0.001]. Patients in Group A were three times less likely to have dehiscence or deep wound infections [0.31 (0.13-0.73); p= 0.007] and fourfold less likely to develop hospital-associated pneumonia [0.25 (0.11-0.58); p< 0.001]. Similarly, the frequencies of major adverse cardiac events (potentially fatal cardiac dysrhythmias, ST elevation myocardial infarction and/or cardiogenic shock) were 5.5-fold lower in Group A compared to those in Group R [0.18 (0.05-0.63); p= 0.004]. Postoperative bleeding was noted in 21.4% of patients in Group R, whereas only 2.7% of patients in Group A developed significant bleeding requiring transfusion (p< 0.001). Postoperative sepsis with or without shock was reported four times less in Group A than in Group R [0.27 (0.12-0.63); p= 0.003]. There were no differences in the prevalence of venous thromboembolism (VTE), acute kidney injury (AKI), urinary tract infection (UTI) or cerebrovascular event (CVE) between the two groups.

Post-procedural death and in-hospital mortality

The unmatched analysis demonstrated improved 30-day survival for geriatric patients with a primary liver tumor who had undergone ablation versus those who had undergone resection (p= 0.043). The mortality rates following tumor ablation and surgical resection were comparable to those predicted by the ACS calculator (Table 3). Cox regression analysis of the matched patients revealed a lower risk of in-hospital mortality in Group A than in Group R [0.33 (0.13-0.83); p= 0.013] (Figure 2A). Subgroup analysis of the matched data further indicated that the risk of in-hospital mortality was much lower after tumor ablation than resection in those with primary hepatic malignancy diagnosis (Figure 2B; p= 0.008). The survival benefit was insignificant among patients with secondary metastatic liver lesions (Figure 2C; p= 0.391).

DISCUSSION

This is the first study comparing liver ablations and resections in a geriatric population. With an aging population, it is essential to garner a better knowledge of how best to treat this patient population and optimize their outcomes. Hepatocellular carcinoma is increasing in incidence and prevalence (10). Considering the average age of diagnosis is 65 years old for HCC, treatment discussion of resection versus ablation is becoming more common. Secondary liver malignancies are also seen more frequently in our aging population.

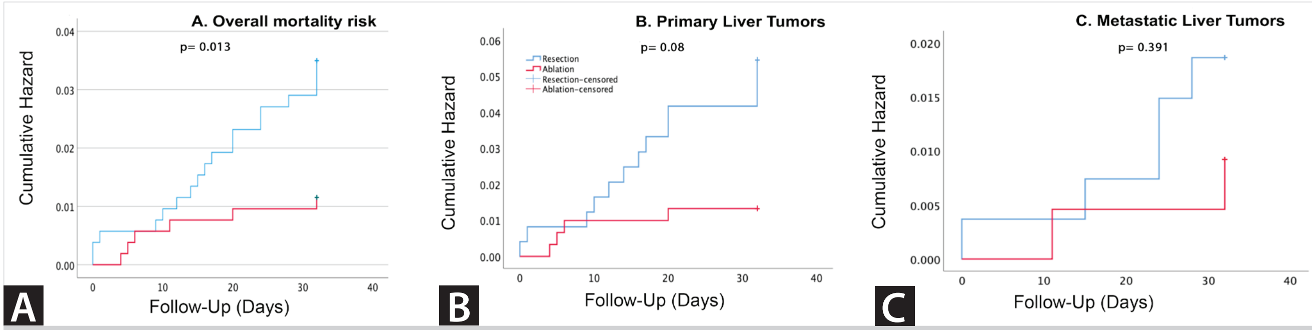

Figure 2. Kaplan-Meier analysis for 30-day mortality of the patients comparing liver ablation and surgical resection. The upper panel **(A)** shows the hazard risk of all patients. The middle panel **(B)** demonstrates the hazard risk between the two treatment groups in the subgroup of patients with primary liver tumors. In contrast, the lower panel **(C)** shows the risk in the subgroup of patients with secondary metastatic tumors of the liver.

There was no difference in sex or age between patients who underwent ablation or resection. However, patients who ultimately had a liver ablation had a higher BMI and a higher number of comorbidities. Preoperative laboratory data for liver enzymes, bilirubin, sodium, and INR portrayed a worse underlying liver function for ablation patients than for resection patients. Despite more comorbidities, obesity, and worse underlying liver function, liver ablation patients had fewer postoperative complications and death rates within 30 days than patients undergoing resection. While ablation patients had lower platelet counts and higher INR, they were less likely to bleed postoperatively than patients treated with resection.

Dedinska and colleagues have demonstrated an improved five-year survival for patients below 65 years of age undergoing liver resection (4). They attribute this difference mainly to the higher prevalence of benign tumors although the scant presence of age-related changes in physiology may have also been a factor. In multivariate analysis, however, they did not find malignancy as a significant risk factor for adverse outcomes. Interestingly, a subset of patients underwent radiofrequency ablation, and their data demonstrated that geriatric patients with ablation had the worst survival.

A single-institution study has compared younger versus older patients undergoing liver resections. There were no differences in severe complications or length of stay, but elderly patients were more likely to be discharged to a rehab facility (11). Another study has looked at age as a risk factor for complications for all abdominal operations for a site-wide database. They have found an increase in postoperative complications and 90-day morbidity in patients of advanced age (2).

Prior studies have compared outcomes following ablation versus resection, but they do not seem limited to elderly patients. A well-conducted meta-analysis has demonstrated that patients with early-stage HCC undergoing liver resection had significantly better long-term disease-free and overall survival (12). These patients likely represent a different patient population from ours, given that they analyzed early-stage HCC. Like our study, they demonstrate that underlying liver disease significantly predicts postoperative outcomes. Another recent meta-analysis has shown no difference in overall survival but lower recurrence-free survival in patients with liver ablation (13). However, patients in this study ranged in mean/median age from 47-71 years. Most were included with preserved liver function (Childs-Pugh class A or B) and single tumors up to 5 cm. The patient population was predominantly Asian. Only one of the included studies was conducted in Europe and non in North America. Post-treatment complications were significantly lower, and the length of stay was significantly shorter in the ablation group. Minimally invasive resection and ablation were compared in a small subset of patients for survival and complications showing similar overall survival and fewer complications in the ablation group. Another report has compared ablations and resections in patients with colorectal metastasis. This study has shown that T4 status, lymph node positivity, and tumor diameter greater than 3 cm portended poorer disease-free survival in the ablation group (14).

There are several limitations to our study. Although these data are derived from the NSQIP database, providing excellent power, there are significant limitations associated with the NSQIP database itself. We cannot separate minimally invasive and open surgeries, and it is possible that more ablations were done laparoscopically than resections, especially in patients with underlying liver disease. Given that these liver resections and ablations were performed for malignant tumors, data on oncologically important variables (clinical stage, margins recurrence-free survival, etc.) would strengthen our findings. We could not examine local recurrence rates, believed to be higher in ablation patients. However, local recurrences have not been demonstrated to translate into worse overall survival in ablation patients but into worse recurrence-free survival more subsequent interventions. We are limited to 30-day mortality and cannot report on long-term survival.

Additionally, there was a fundamental difference between the treatment groups, which could not be adjusted even with PSM. Due to the retrospective nature of this study, group allocation was based on the patient's physical condition and the risk of a given procedure at the time of treatment. Any further attempt to expand the PSM to include the laboratory values results in no matched patients between the two groups. Although patients were even more fragile in group A than in group R, the survival benefit and lower risk postoperative complication compel the choice of tumor ablation in treating liver lesions <5 cm in diameter in severely ill patients.

CONCLUSION

Patients undergoing liver ablation had more comorbidities, worse underlying liver function and lower in-hospital mortality. For primary liver malignancies, resection had a significantly worse 30-day survival. Underlying liver disease is an essential determinant of postoperative complications, and special consideration should be given to liver function when choosing between surgical treatment modalities for elderly patients.

Ethics Committee Approval: The research utilized a retrospective cohort study design, drawing data from the American College of Surgeons National Surgical Quality Improvement Program, which is open to the public and the participating institutions. The study uses unidentified information and it was exempted from Institutional Review Board regulation.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - CG, NN; Design - CR, NN; Supervision - , CG, SS; Fundings - SS, NN; Data Collection and/or Processing - GS, NN; Analysis and/or Interpretation - CR, CG, NN; Writing Manuscript - CR, CG, NN; Critical Reviews - CG, SS, NN.

Conflict of Interest: The authors have no conflicts of interest to declare.

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ORİJİNAL ÇALIŞMA-ÖZET
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Geriyatrik hastalarda ablasyon ile karaciğer rezeksiyonunun karşılaştırması - yöntemlerden biri hastane içi mortaliteyi iyileştirir mi?

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ÖZET

Giriş ve Amaç: Bu çalışmanın amacı karaciğer malignitelerinin tedavisinde 65 yaş ve üzeri hastalarda cerrahi rezeksiyon ile ablasyonu karşılaştırmaktı.

Gereç ve Yöntem: Karaciğer tümörlü vakalar NSQIP veri tabanından 65 yaş üstü hastalar olarak alındı. Eğilim skoru eşleştirmesinin ardından, karaciğer rezeksiyonu ve ablasyonu için 30 günlük morbidite ve mortalite için çok değişkenli Cox regresyonu kullanıldı.

Bulgular: Eğilim skoru eşleştirmesinin ardından, 1048 hasta komorbid durumlar için 1:1 eşleştirildi. Hastalar rezeksiyondan sonra üç gün daha uzun süre hastanede kaldı (p< 0,001). Ablasyon sonrasında mortalite daha düşüktü (p= 0,013). Bu fark primer karaciğer tümörü olan hastalarda daha belirgindi (p= 0,008). Grup A'da abdominal apse gelişme riski 10 kat, hastane ilişkili pnömoni (p= 0,001) ve yeniden entübasyon riski dört kat, transfüzyon gerektiren kanama riski 10 kat (p< 0,001) ve sepsis gelişme riski üç kat (p< 0,001) daha düşüktü.

Sonuç: Genel olarak daha hasta ve altta yatan karaciğer fonksiyonu daha kötü olan bir hasta popülasyonu olmasına rağmen ablatif teknikler karaciğerin primer malin tümörlerinin daha agresif rezeksiyonu ile karşılaştırıldığında daha düşük komplikasyon riski ile ilişkilendirilmiştir.

Anahtar Kelimeler: Karaciğer kanseri, rezeksiyon, ablasyon, komplikasyonlar

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