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Evolving Treatment Strategies and Management Protocols for Spontaneously Ruptured Hepatocellular Carcinomas: A 30-Year Comparative Analysis

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Background

Spontaneous rupture of hepatocellular carcinoma (srHCC) is a life-threatening complication with poor prognoses, requiring urgent intervention to achieve hemostasis. Despite advancements in treatment, the optimal management strategy remains debated, particularly regarding patients' long-term survival outcomes and the relative efficacy of different treatment modalities.

Methods

This retrospective study analyzed 444 patients diagnosed with srHCC from 1991 to 2020, categorized into three periods: 1991-2000 (Period 1), 2001-2010 (Period 2), and 2011-2020 (Period 3). Interventions included conservative management, transarterial embolization (TAE), surgical interventions, and radiofrequency ablation (RFA).

The primary endpoints of the study were short-term mortality rates at 30 and 90 days, as well as long-term survival rates at 3 years. A multivariate analysis was performed to identify prognostic factors influencing survival outcomes.

Objectives

This study evaluates the evolution of srHCC management over 30 years and its impact on patient outcomes at the Queen Mary Hospital, a tertiary center in Hong Kong.
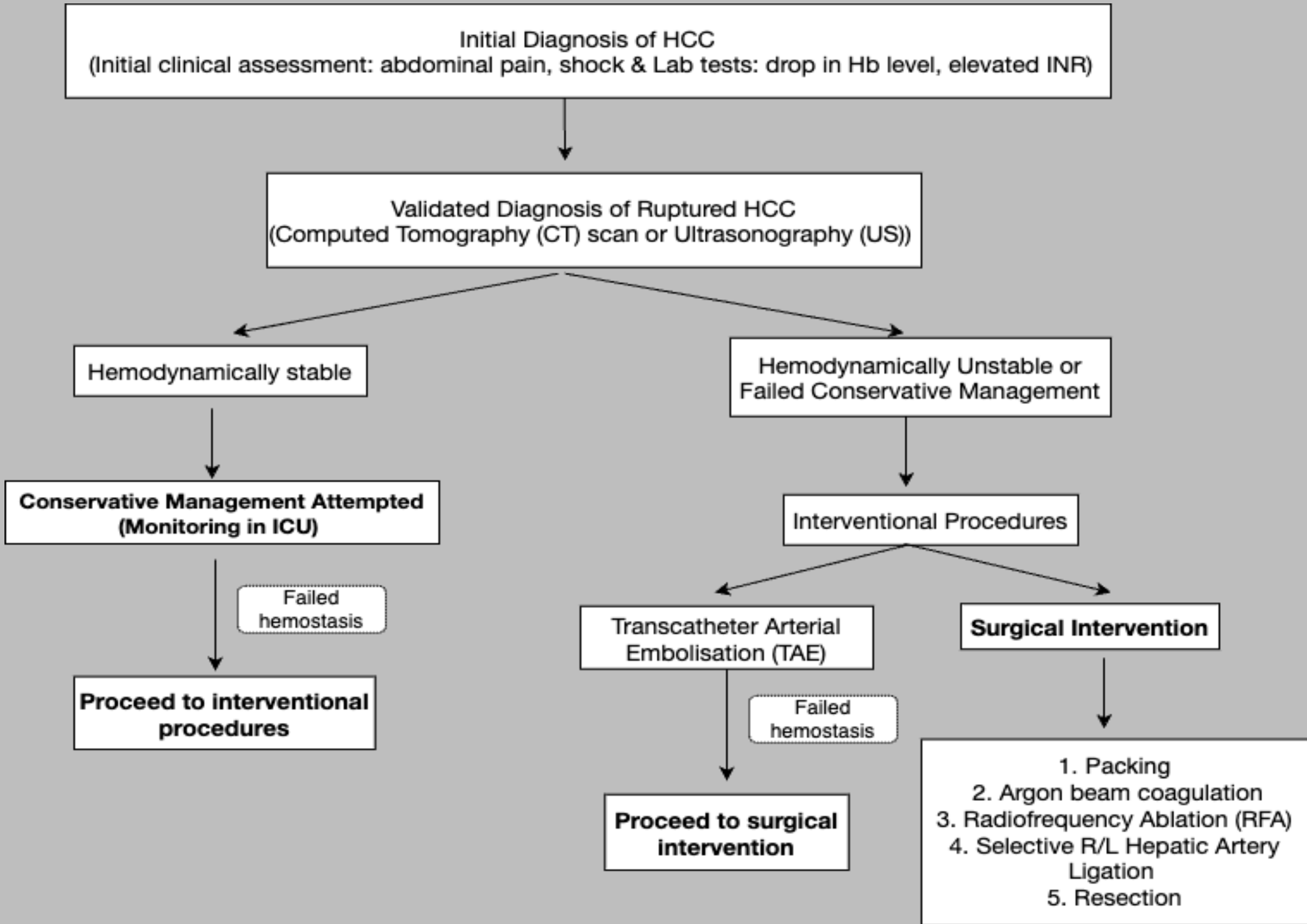

Fig. 1. Current Refined Treatment Algorithm on Spontaneous Ruptured Hepatocellular Carcinoma (srHCC)
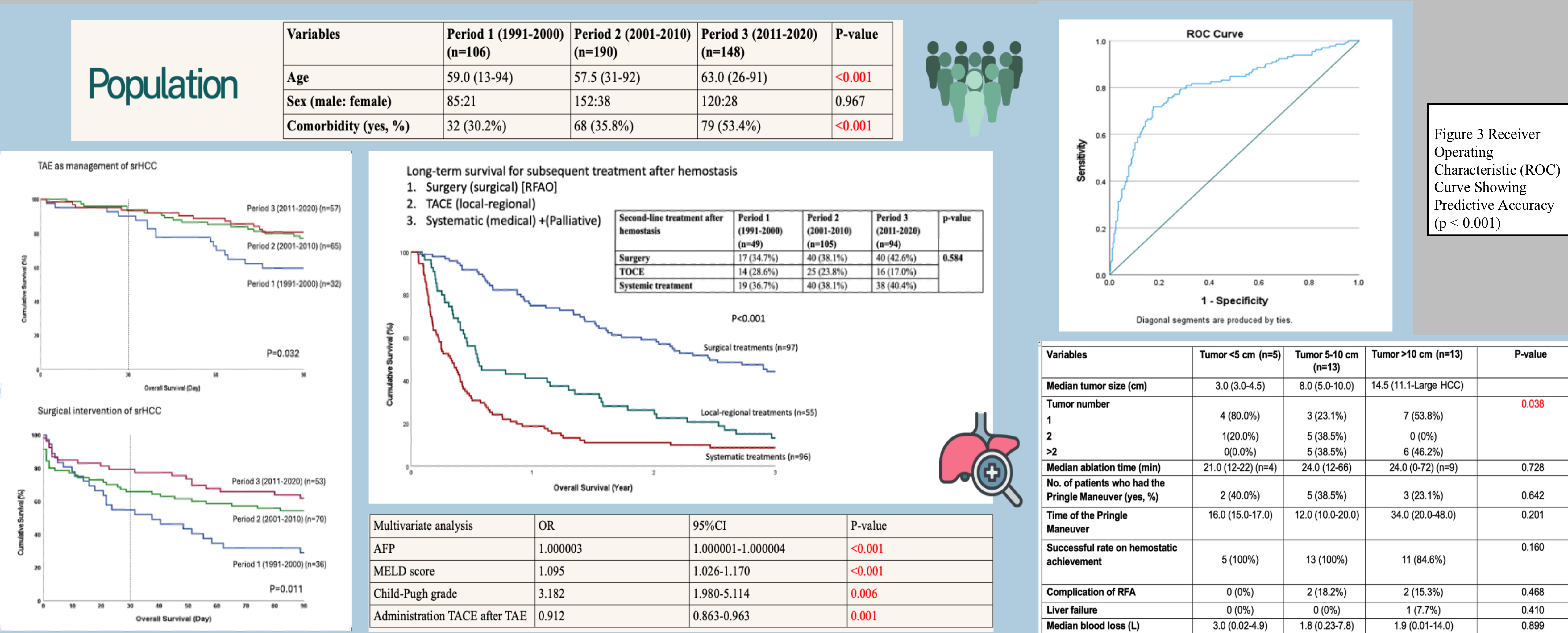
Results

Population

Variables	Period 1 (1991-2000) (n=106)	Period 2 (2001-2010) (n=190)	Period 3 (2011-2020) (n=148)	P-value
Age	59.0 (13-94)	57.5 (31-92)	63.0 (26-91)	<0.001
Sex (male: female)	85:21	152:38	120:28	0.967
Comorbidity (yes, %)	32 (30.2%)	68 (35.8%)	79 (53.4%)	<0.001

Figure 3 Receiver Operating Characteristic (ROC) Curve Showing Predictive Accuracy (p < 0.001)

Long-term survival for subsequent treatment after hemostasis
1. Surgery (surgical) [RFAO]
2. TACE (local-regional)
3. Systematic (medical) +(Palliative)

Second-line treatment after hemostasis	Period 1 (1991-2000) (n=49)	Period 2 (2001-2010) (n=105)	Period 3 (2011-2020) (n=94)	p-value
Surgery	17 (34.7%)	40 (38.1%)	40 (42.6%)	0.584
TOCE	14 (28.6%)	25 (23.8%)	16 (17.0%)	
Systemic treatment	19 (36.7%)	40 (38.1%)	38 (40.4%)	

Multivariate analysis	OR	95%CI	P-value
AFP	1.000003	1.000001-1.000004	<0.001
MELD score	1.095	1.026-1.170	<0.001
Child-Pugh grade	3.182	1.980-5.114	0.006
Administration TACE after TAE	0.912	0.863-0.963	0.001

Figure 2. Overall Survival Rates of patients with srHCC with multivariate analysis

Variables	Tumor <5 cm (n=5)	Tumor 5-10 cm (n=13)	Tumor >10 cm (n=13)	P-value
Median tumor size (cm)	3.0 (3.0-4.5)	8.0 (5.0-10.0)	14.5 (11.1-Large HCC)	
Tumor number				0.038
1	4 (80.0%)	3 (23.1%)	7 (53.8%)	
2	1(20.0%)	5 (38.5%)	0 (0%)	
>2	0(0.0%)	5 (38.5%)	6 (46.2%)	
Median ablation time (min)	21.0 (12-22) (n=4)	24.0 (12-66)	24.0 (0-72) (n=9)	0.728
No. of patients who had the Pringle Maneuver (yes, %)	2 (40.0%)	5 (38.5%)	3 (23.1%)	0.642
Time of the Pringle Maneuver	16.0 (15.0-17.0)	12.0 (10.0-20.0)	34.0 (20.0-48.0)	0.201
Successful rate on hemostatic achievement	5 (100%)	13 (100%)	11 (84.6%)	0.160
Complication of RFA	0 (0%)	2 (18.2%)	2 (15.3%)	0.468
Liver failure	0 (0%)	0 (0%)	1 (7.7%)	0.410
Median blood loss (L)	3.0 (0.02-4.9)	1.8 (0.23-7.8)	1.9 (0.01-14.0)	0.899

Table 1 Operation details of RFA for hemostasis

Discussion

- **Advancements in Management**:
Shift from predominantly surgical interventions to minimally invasive approaches such as TAE, TACE, and RFA.
- **Improved Outcomes**:
Decreasing 30-day and 90-day mortality rates and increasing three-year survival rates demonstrate the impact of evolving treatment strategies.
- **Key Risk and Protective Factors**:
Factors including large tumor size, high AFP levels, and poor liver function remain critical risks, while interventions like TACE following TAE and resection hemostasis showed protective benefits.
- **Challenges**:
Persistent complications such as liver failure post-RFA and the retrospective nature of the study limit broader applicability and comparability of findings.

Conclusion

- **Significant Progress**:
Advancements in imaging, surgical techniques, and minimally invasive interventions have markedly improved patient outcomes for srHCC over the last three decades.
- **Future Directions**:
Prospective studies and personalized approaches tailored to patient-specific risk profiles are necessary to further refine treatment strategies.
- **Remaining Challenges**:
Focus on enhancing the safety and efficacy of minimally invasive treatments and addressing complications related to advanced liver disease and comorbidities.
- **Potential for Innovation:**
Integration of TACE into treatment protocols offer opportunities to enhance survival.

Acknowledgements

Calculation

Krystal-Wallis H test was used to compare continuous variables. Pearson's Chi-square test for independence was used to study the association between discrete data. Survival analyses were performed using the Kaplan-Meier method, with group comparisons conducted via the log-rank test.