Symposium on Clinical Interventional Oncology

Interventional Oncology Procedures with Adjuvant Adoptive Cell Therapy in the Treatment of Hepatocellular Carcinoma

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Background and Introduction

Hepatocellular carcinoma (HCC) is the sixth most common cause of cancer and the third leading cause of cancer-related death globally[1]. Chronic inflammation in hepatocellular carcinoma generates a niche microenvironment that produces immune exhaustion and evasion and is attributed to its high recurrence rate. Several immunotherapy options for HCC treatment are often used in the intermediate and advanced stages—checkpoint inhibitors such as atezolizumab, durvalumab, and tremelimumab aim to overcome immune fatigue. However, the results are underwhelming for HCC[2,3].

Adoptive cell therapy (ACT) is a form of immunotherapy that utilizes the transfer of activated immune cells to produce an antitumor immune response in patients. Cytokine-induced natural killer cells (CIK) are a form of activated NK cells that are readily producible by drawing peripheral mononuclear cells from patients, stimulating them in vitro with cytokines, and infusing them back into the patient[4]. Combining interventional oncology (IO) procedures and adjuvant adoptive cell therapy is a proposed mechanism for bolstering the immune system to eradicate tumors, prevent immune evasion, and reduce progression.

This literature review aims to evaluate studies assessing the safety and efficacy of minimally invasive IO procedures in combination with adjuvant adoptive cell therapy in treating patients with HCC.

Methods

A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure 1) to determine studies that addressed adjunctive ACT with minimally invasive interventional use oncologic procedures in patients with HCC. An electronic search was conducted through PubMed and EBSCOhost. Abstracts within search terms were screened using eligible criteria, including adoptive cell therapy, a minimally invasive oncologic procedure, and human participants with hepatocellular carcinoma. The primary endpoints were to assess the efficacy and safety between interventional oncology therapy only and combination therapy.

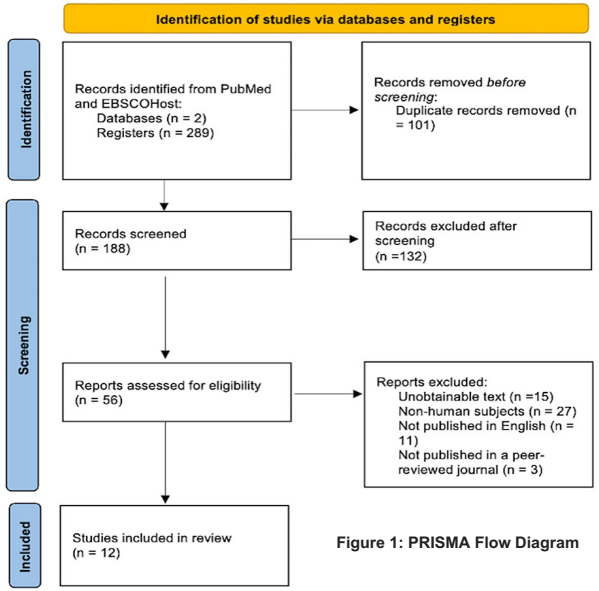

Figure 1: PRISMA Flow Diagram

Results

Multiple studies evaluated in this review found **statistically significant increases in the median Overall Survival (OS) and median Progression-Free Survival (PFS) rates in the combined therapy compared to control group receives only the interventional oncology procedures** (Table 1).

No severe complications or mortalities were reported in either group. **Patients who receive the combination therapy are significantly more likely to develop fever as a side effect than patients who receive only the IO procedures (27.29% vs. 5.32%, p = 0.0027).** No statistical significance was found in other documented adverse events such as pleural effusion, fatigue, abdominal pain, or ascites.

Several studies have found a significant increase in CD8+ cells and one study found an increase in the number of lymphocytes and pro-inflammatory cytokines such as IFN-gamma in combination therapy.

Median Overall Survival (Months)				
Study	Combination Therapy	Control Group	Experimental Group	P value
Yang et, al. 2018	NK cell and IRE	17.6	23.2	0.031
Alnaggar et al. 2018	NK and IRE	8.9	10.1	0.0078
He et al. 2016	NK + DC and TACE	13.3	24.8	< 0.001
Huang et al. 2013	NK and TACE + RFA	31.0	56.0	0.023
Huang et al. 2020	NK and TACE + MWA	24.0	41.0	0.002
Average Overall		19.0	31.0	
Median Progression-Free Survival (Months)				
Study	Combination Therapy	Control Group	Experimental Group	P value
Yang et al. 2018	NK and IRE	10.6	15.1	0.018
Huang et al. 2020	NK and TACE + MWA	10.0	12.0	0.216
Huang et al. 2013	NK and TACE+RFA	10.0	17.0	< 0.001
Weng et al. 2008	NK and TACE+RFA	15.0	16.8	0.012
Cui et al. 2013	NK and RFA	12.0	28	-
Lin et al. 2017	NK and Cryoablation	7.6	9.1	0.01
Pan et al. 2010	NK and TACE +RFA	6.8	10.2	-
Average Overall		10.3	15.5	

Table 1. Evaluation of Efficacy and Prognosis

Conclusions

This review suggests that IO procedures combined with adjuvant natural killer cell immunotherapy are equally safe and effective as IO procedures alone in treating hepatocellular carcinoma patients. The combination therapy groups had significantly higher median overall survival and progression-free survival rates than the control groups. The two types of therapies have demonstrated equivalent safety with no complications or mortalities reported, although patients who receive the combination therapy are significantly more likely to develop fever as a side effect than patients who receive only the IO procedures.

References

1.Sung, H. *CA: a Cancer Journal for Clinicians*, *71*(3), 209–249. https://doi.org/10.3322/caac.21660
2.Onuma, A. E. Gene Expression, 20(1), 53–65. https://doi.org/10.3727/105221620X15880179864121
3.Liu, X. The Oncologist (Dayton, Ohio), 24(S1), S3–S10. https://doi.org/10.1634/theoncologist.2019-IO-S1-s01
4.Fu, Y. Journal of Experimental & Clinical Cancer Research, 38(1), 396–396. https://doi.org/10.1186/s13046-019-1396-4