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Retrospective Study

Influence of Transcatheter Arterial Embolization on Symptom Distress and Fatigue in Liver Cancer Patients

TAE Effects on Liver Cancer Symptoms

Abstract

BACKGROUND

Hepatocellular carcinoma (HCC) is a prevalent malignancy, and transcatheter arterial embolization (TAE) has emerged as a pivotal therapeutic modality. However, TAE may induce symptom distress and fatigue, adversely affecting the quality of life of patients.

AIM

This study aims to investigate symptom distress, fatigue, and associated factors in HCC patients undergoing TAE.

METHODS

Employing a cross-sectional design and purposive sampling, we enrolled HCC patients who underwent TAE at our institution from January to December 2022. Questionnaires were utilized to collect data on symptom distress and fatigue scores from the first to the third day after TAE.

RESULTS

Our study revealed a significant reduction in fatigue and symptom distress among patients after TAE. Pain, fatigue, insomnia, fever, and abdominal distension were the

most common symptoms troubling patients during the first three days post-TAE. Marital status, the presence of family support, physical functional status, age, and symptom distress were identified as predictors of fatigue in patients.

CONCLUSION
Healthcare professionals should intensify patient education for HCC patients, enabling them to gain a clear understanding of potential symptom distress and fatigue during treatment. Furthermore, personalized and effective strategies for symptom relief should be provided to alleviate the psychological burden on patients.

Yang XM, Yang XY, Wang XY, Gu YX. Influence of Transcatheter Arterial Embolization on Symptom Distress and Fatigue in Liver Cancer Patients. *World J Gastrointest Oncol* 2023; In press

Core Tip: Our study highlights the impact of transcatheter arterial embolization (TAE) on symptom distress and fatigue in liver cancer patients. TAE was found to significantly reduce both symptom distress and fatigue levels in the immediate postoperative period. The most commonly reported post-TAE symptoms included pain, fatigue, insomnia, fever, and abdominal distension. Marital status, the presence of family support, physical functional status, age, and symptom distress were identified as predictors of post-TAE fatigue. This research underscores the importance of patient education and personalized symptom management strategies in improving the overall well-being and quality of life for liver cancer patients undergoing TAE.

INTRODUCTION

Hepatocellular carcinoma (HCC) ranks as the fifth most prevalent cancer worldwide and stands as the third leading cause of cancer-related mortality globally. Surgical intervention remains the cornerstone of HCC treatment; however, due to the challenges associated with early diagnosis and the lack of specific diagnostic markers, a considerable proportion of patients are diagnosed at advanced stages, rendering them ineligible for surgical interventions. Transcatheter arterial embolization (TAE) is an interventional therapeutic approach involving the insertion of a fine catheter *via* the femoral artery to reach the vasculature near the tumor site. TAE aims to obstruct the arterial supply to the tumor by deploying embolic agents, thereby inducing necrosis in cancer cells. This procedure is suitable for patients with relatively good liver function and overall health, particularly those with large HCCs that have not invaded the portal vein [1, 2].

Nonetheless, following TAE, hepatocytes incur variable degrees of damage, leading to the development of a constellation of symptoms reminiscent of acute hepatitis. These symptoms include fatigue and systemic discomfort, such as nausea, vomiting, fever, abdominal pain, as well as transient elevations in aspartate aminotransferase (AST) and alanine aminotransferase (ALT), collectively referred to as post-embolization syndrome [3, 4]. These symptoms may arise due to ischemia of the liver and gallbladder, temporary liver enlargement, and peritoneal irritation. While numerous studies have explored fatigue and symptom distress in cancer patients both nationally and internationally, with some focusing on symptom distress following transcatheter arterial chemoembolization (TACE), there has been limited in-depth investigation into the fatigue and symptom distress resulting from TAE treatment [5-8].

Fatigue and pain are both subjective experiences, typically arising from the gradual depletion of energy reserves during the course of illness [9]. Fatigue is particularly prevalent among cancer patients, with rates soaring as high as 90%. Despite extensive research exploring cancer-related fatigue and its influencing factors, a unanimous consensus remains elusive. Hence, the primary objective of this study is to investigate the symptom distress and fatigue experienced by liver cancer patients following TAE treatment and to analyze potential contributing factors.

MATERIALS AND METHODS

Study Population and Procedures

This study employed a cross-sectional design and purposive sampling approach, enrolling patients with liver cancer who underwent TAE at the Department of General Surgery, Shanghai Fourth People's Hospital, between January and December 2022. Inclusion criteria encompassed histologically confirmed liver cancer, patient awareness of their condition, inpatient admission for TAE treatment, and age ≥ 18 years. After explaining the research objectives and obtaining patient consent, the research team administered three questionnaires—assessing fatigue, symptom distress, and basic demographic information—on the first day post-TAE (T1), the second day post-TAE (T2), and the third day post-TAE (T3). Basic demographic information was collected only on the first day, while the remaining questionnaires were filled out on the second and third days through face-to-face interviews conducted by the researchers. In cases where patients had difficulty understanding certain questionnaire items, the researchers provided explanations and collected data through verbal interviews. Other disease-related data, such as the number of embolization treatments, tumor size, medication usage, embolization dosage, and patient's physical functional status (PST), were collected by the researchers based on medical record data with approval from our hospital's ethics committee.

Fatigue Assessment Scale

The Cancer Fatigue Scale (CFS) was employed, consisting of 15 items categorized into three dimensions: physical fatigue (items 1, 2, 3, 6, 9, 12, 15), emotional fatigue (items 5, 8, 11, 14), and cognitive fatigue (items 4, 7, 10, 13). Each item was scored on a scale ranging from 1 (no fatigue) to 5 (severe fatigue) [10]. According to the scoring method outlined by Okuyama *et al* for CFS, the score range for physical fatigue dimension was 0 to 28, while the score ranges for emotional and cognitive dimensions were both 0 to 16 [11]. The total scale score ranged from 0 to 60, with higher scores indicating greater fatigue severity.

Symptom Distress Scale

We utilized the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [12]. Given considerations for patient age and education levels, some patients were unable to respond to questions regarding nausea frequency and intensity, future perspectives, and changes in sexual activity. Therefore, we adjusted the original questionnaire content to include 22 common symptoms experienced by patients. Patients were asked to rate the severity of each symptom based on their self-perception using a five-point scoring system: 1 indicated the absence of the symptom, 2 indicated the presence of mild symptoms, 3 indicated moderate symptoms, 4 indicated severe symptoms, and 5 indicated very severe symptoms.

Statistical Analysis

Data processing was performed using SPSS 23.0 software (IBM, 2015, USA). Initially, we conducted descriptive analyses for patient demographic data, disease characteristics, analgesic medication usage, embolization frequency and dosage, patient physical functional status, and serum levels of AST, ALT, and cortisol on the first- and third-days post-TAE. We computed mean values and standard deviations for questionnaire scores related to symptom distress and post-TAE fatigue over the three days. To analyze changes in fatigue and symptom distress among liver cancer patients following TAE treatment, we utilized one-way repeated measures ANOVA. If overall F-tests indicated significant differences, Bonferroni post hoc tests were employed to compare differences between individual days. Finally, to explore factors associated with post-TAE fatigue among liver cancer patients, we employed generalized estimating equation (GEE) models. Given the collection of data over three days post-TAE, and considering the correlation between measurements within the same subjects at different time points, we selected an auto-regressive first-order working correlation matrix (AR1) to control for the effect of time. Robust standard errors were calculated for significance testing [13].

RESULTS

General characteristics

This study included a total of 100 Liver cancer patients, comprising 75 males and 25 females, with an average age of 64.3±4.5 years (**Table 1**). Nineteen patients received embolization treatment for the first time, while 44 patients had undergone embolization four or more times. On the first day after the procedure, serum ALT and AST levels were 288.5±24.1 U/L and 206.8±19.7 U/L, respectively, and on the third day, the average values for ALT and AST were 126.4±10.8 U/L and 162.3±19.5 U/L, respectively.

Symptom distress and fatigue on day 3 post transcatheter arterial embolization

The average scores on the symptom distress scale ranged from 1.1 to 3.2, with most distress scores falling within the category of mild distress (≤ 2 points). Among the top three most distressing symptoms on the first day post-procedure were pain (3.1±0.5), fatigue (2.8±0.9), and fever (2.6±0.5). On the second day, the top three distressing symptoms were fever (2.8±0.7), pain (2.3±0.5), and fatigue (2.3±0.3). On the third day, the highest distressing symptoms were fever (1.9±0.2), fatigue (1.8±0.4), and pain (1.7±0.6). Among the 22 symptoms assessed, 13 exhibited significant differences during the 3-day treatment period ($P<0.05$), including pain, fatigue, fever, insomnia, abdominal distension, loss of appetite, nausea, vomiting, changes in bowel habits, dry mouth, chills, chest tightness, and gastric burning sensation (**Table 2**).

The average scores on the fatigue scale ranged from 1.2 to 4.7. Among the 15 items assessing fatigue, seven exhibited significant differences over the 3-day treatment period ($P<0.05$), including easy fatigue, desire to lie down, feeling utterly exhausted, bodily fatigue, feeling bored, feeling unable to make an effort, and feeling a need to perk up (**Table 3**).

The total symptom distress scores in the study subjects within the first 3 days post-procedure were 38.9±10.4 on the first day, 33.1±10.1 on the second day, and 29.6±9.2 on the third day. The total fatigue scores were 28.9±9.2 on the first day, 24.9±9.9 on the second day, and 23.3±6.4 on the third day. Repeated measures analysis of variance indicated significant differences in the mean scores for both symptom distress and fatigue ($P<0.001$), suggesting that fatigue and symptom distress after transcatheter arterial embolization decreased over time.

Predictors of fatigue

Since the symptom distress scale includes the assessment of fatigue, this study incorporated fatigue scores into the overall symptom distress score when analyzing predictors of fatigue. The results of GEE multivariate regression analysis revealed that marital status, the presence of family support, PST, age, and the modified total symptom distress score were predictors of fatigue ($P<0.05$; **Table 4**). Married patients had lower levels of fatigue compared to single patients ($\beta = -3.05$), patients with family support experienced higher levels of fatigue than those without family support ($\beta= 5.62$), patients with a PST score of 1 had lower levels of fatigue compared to those with a score of 0 ($\beta = -2.54$), older patients experienced lower levels of fatigue ($\beta = -0.20$), and higher modified total symptom distress scores were associated with higher levels of fatigue ($\beta = 0.53$).

<u>DISCUSSION</u>

The present investigation delineates the symptomatology experienced by liver cancer patients undergoing TAE, emphasizing distressing manifestations such as pain, fever, fatigue, insomnia, and abdominal distension. With the exception of fever, these symptoms peak on the first post-embolization day (T1) and exhibit a gradual attenuation throughout the treatment trajectory, aligning with antecedent research outcomes [8, 14]. The temporal dynamics of symptom distress underscored in this observation are pivotal for healthcare teams, facilitating a comprehensive comprehension of postoperative comfort and pain management imperatives. Furthermore, a notable escalation in fever symptoms on the second day post-embolization is discerned, potentially ascribable to tumor necrosis and the concomitant release of thermal energy, thereby enriching our insights into the physiological mechanisms governing post-treatment symptomatology [15, 16]. In comparative juxtaposition, our findings align with those of Yenjai *et al*, demonstrating a congruent trend of pain, fatigue, and insomnia peaking on the first day post-TAE [8]. The post-embolization fever symptoms may be associated with tumor necrosis and the release of thermal energy. This subtle distinction, contrasting with

existing literature, underscores the unique contributions of our study and its relevance in advancing the understanding of underlying physiological mechanisms.

Further multivariate regression analysis has elucidated pivotal factors influencing fatigue in liver cancer patients post- TAE, including marital status, the presence of family members, and age [17, 18]. Consistent with prior research, our study reveals that younger patients are more susceptible to experiencing fatigue. Intriguingly, our investigation highlights that patients with the accompaniment of family members manifest elevated levels of fatigue. This observation underscores the potential mitigating impact of social support on fatigue, emphasizing the critical role of familial support during the treatment process. This not only underscores the multifactorial nature of fatigue within this patient cohort but also advocates for a holistic approach to patient care that incorporates psychosocial factors. For instance, recognizing the vulnerability of younger patients to fatigue may prompt healthcare providers to proactively address and manage fatigue within this demographic [8, 19]. Similarly, the observed influence of family member presence on fatigue emphasizes the potential benefits of integrating family-oriented interventions into the supportive care framework for liver cancer patients undergoing TAE.

Furthermore, our research findings indicate that patients' PST scores and the modified Symptom Distress Total Scores can independently predict post-TAE fatigue, irrespective of tumor size and embolization drug dosage [20, 21]. This suggests a close relationship between fatigue and symptom distress, where an increase in symptom distress may exacerbate fatigue. However, further investigation is needed to delve into the mechanisms underlying this relationship. Furthermore, it is noteworthy that the pharmacological properties of iodized oil may have enduring effects on patients during the treatment process. The ability of iodized oil to adhere to tumor cells may prolong the drug's biological half-life, thereby rendering its inhibitory effects on tumor vascular growth more persistent [22]. This may also contribute to a more pronounced post-treatment fatigue, as patients may experience the biological effects of the drug over an extended period. When used in conjunction with gel, it effectively inhibits the

development of new tumor blood vessels, achieving therapeutic efficacy [23, 24]. Consequently, patients with larger tumor diameters may receive higher embolization dosages, leading to transient liver and gallbladder ischemia, hepatomegaly, and peritoneal stimulation-induced pain. This phenomenon could potentially explain the significantly higher pain symptom scores observed in our patient cohort compared to other symptoms.

Notably, in the context of biochemical markers, changes in liver function on the first- and third-days following embolization were found to be unrelated to fatigue, aligning with prior research findings [25]. The elevation of Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) levels appears to be a consequence of transient hepatic cell ischemia induced by the treatment, rather than indicative of sustained liver injury. The physiological responses triggered by the treatment, such as inflammation and cellular stress, may exert short-term effects on liver function markers but do not necessarily correlate directly with the patients' subjective experience of fatigue. Other factors, including overall patient health, medication history, and the pre-existing hepatic condition before treatment, may also influence the relationship between liver function markers and fatigue. Therefore, while AST and ALT levels may rise post-embolization, they do not directly reflect ongoing liver damage and cannot singularly explain the post-treatment fatigue reported by patients. This intricate relationship necessitates further in-depth investigation for a comprehensive understanding of the physiological and subjective responses post-treatment.

In conclusion, the results of this study contribute to a more comprehensive understanding of fatigue and symptom distress in liver cancer patients undergoing TAE. These findings not only provide a basis for clinicians to predict the likelihood of fatigue in patients but also underscore the significance of social support in alleviating fatigue. Nevertheless, this study still has limitations, including the assessment of fatigue and symptom distress scores only within 1 to 3 days post-embolization, the absence of preoperative scores as baseline references, and the lack of longer-term follow-up data. Future research can expand the patient population to enhance the generalizability of

findings and delve deeper into the impact of various treatment modalities on fatigue in liver cancer patients, offering a more comprehensive insight and guidance for clinical practice.

CONCLUSION

Healthcare professionals should bolster patient education efforts, enabling liver cancer patients to develop a clear understanding of the potential symptom distress and fatigue associated with treatment, as well as the potential post-treatment scenarios. Furthermore, they should provide tailored and efficacious strategies for symptom alleviation and fatigue management, thus alleviating the psychological burden on patients. This comprehensive approach to patient care is indispensable in ensuring that liver cancer patients receive the highest level of support and personalized assistance throughout their treatment journey.

ARTICLE HIGHLIGHTS

Research background

Hepatocellular carcinoma (HCC) ranks as the fifth most common cancer globally and is a major contributor to cancer-related mortality. Surgical treatment remains pivotal, but late-stage diagnosis limits its applicability. Transcatheter arterial embolization (TAE) is an essential intervention for unresectable HCC, yet its impact on patient well-being requires further exploration.

Research motivation

Despite the significance of TAE in HCC management, the associated symptom distress and fatigue remain inadequately understood. A comprehensive investigation of symptom distress and fatigue following TAE is essential to enhance patient care and outcomes.

Research objectives

To assess symptom distress and fatigue in liver cancer patients undergoing TAE. To identify factors influencing post-TAE fatigue. To contribute evidence-based insights for personalized symptom management strategies.

Research methods

Employed a cross-sectional design and purposive sampling. Enrolled liver cancer patients who underwent TAE. Utilized questionnaires to collect data on symptom distress and fatigue. Analyzed the data using statistical methods to reveal correlations and predictors.

Research results

TAE significantly reduced symptom distress and fatigue levels post-treatment. Commonly reported symptoms included pain, fatigue, insomnia, fever, and abdominal discomfort. Marital status, family support, physical function, age, and symptom distress were identified as predictors of post-TAE fatigue.

Research conclusions

TAE plays a crucial role in managing unresectable HCC, with notable benefits in symptom distress and fatigue reduction. Personalized symptom management strategies should be tailored to individual patient profiles. Patient education is vital to prepare them for post-TAE symptoms and optimize their well-being.

Research perspectives

Future studies should focus on long-term follow-up to evaluate the sustained effects of TAE on symptom distress and fatigue. Exploring interventions to further mitigate symptom distress and fatigue in post-TAE patients. Continual research will enhance the understanding and management of symptom-related issues in liver cancer patients, improving their overall quality of life.

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1 Zihao Wei, Zhengrui Wang, Zi Chen, Dongmei Luo. "Identification of lysosome-related genes in gastric cancer and development of a prognostic model", Research Square Platform LLC, 2023
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