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Efficacy and Safety of Drug Elution Bead-Transarterial Chemoembolization in Advanced Soft Tissue Sarcoma

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Abstract: Soft-tissue sarcomas (STS) are rare and heterogeneous tumors originating from mesenchymal tissues. While surgical resection remains the primary treatment, not all patients are eligible for surgery, particularly in advanced stages. Drug-eluting bead transarterial chemoemboli zation (DEB-TACE) is a promising therapeutic option for such cases. This retrospective study evaluated the efficacy and safety of DEB-TACE in 30 patients with advanced STS at Prof. Dr. R. D. Kandou Hospital, Manado, from 2020 to 2023. The overall response rate (ORR) was 76.7% ($p<0.05$), with five patients achieving complete response and 18 showing partial response. The main adverse reactions included post-embolization syndrome (fever, pain, nausea, vomiting) and grade II or higher bone marrow suppression. Despite a morbidity rate of 93.3%, no treatment-related mortality was observed. In conclusion, DEB-TACE is an effective and safe treatment for advanced STS, providing superior short-term efficacy compared to traditional systemic chemotherapy.
Keywords: soft tissue sarcoma; drug eluting bead; transarterial chemoembolization

INTRODUCTION

Soft tissue sarcomas (STS) are a rare and diverse group of malignant tumors that originate from mesenchymal tissues such as muscle, fat, blood vessels, and connective tissues. Although these tumors represent only about 1% of all adult malignancies, their heterogeneity and complex biological behaviors make them a significant clinical challenge. There are over 100 distinct histological subtypes of STS, each exhibiting different degrees of aggressiveness, rates of metastasis, and responses to treatment. Due to their diverse origins, STS can occur in various locations in the body, complicating diagnosis and treatment strategies. Some of the most common subtypes include liposarcomas, leiomyosarcomas, and synovial sarcomas, but their relative rarity has limited large-scale clinical studies, making treatment protocols more challenging to standardize.[1]

The primary treatment modality for localized STS is surgical resection, particularly when complete removal of the tumor with wide margins is feasible. Surgical excision provides the best chance for long-term survival, as complete resection can achieve local control of the disease and reduce the risk of recurrence. However, up to 50% of patients present with advanced disease that is not amenable to surgery, either due to tumor location or metastasis at the time of diagnosis. In these cases, non-surgical interventions, such as systemic chemotherapy, are often employed as the primary treatment option. Unfortunately, the outcomes of systemic chemotherapy in STS patients have been suboptimal, with modest improvements in survival rates and significant treatment-related toxicities. Chemotherapy's limited efficacy in advanced or metastatic cases has spurred interest in alternative treatment approaches that can provide more targeted and localized therapy.[2]

One of the primary challenges in treating STS is the heterogeneous nature of these tumors, both in their histology and in their responses to chemotherapy.[2] Unlike more common cancers, where robust clinical trials have established standardized chemotherapy regimens, STS lacks a "one-size-fits-all" approach due to the differences in tumor biology across subtypes. The use of anthracyclines, such as doxorubicin, as first-line chemotherapy has demonstrated moderate activity in certain STS subtypes, but the associated systemic toxicities, including cardiotoxicity, limit its utility in many patients. This has led to a growing interest in more localized and targeted treatment modalities that can enhance the efficacy of chemotherapy while minimizing systemic side effects.[3]

Transarterial chemoembolization (TACE) has gained increasing attention as an alternative therapeutic approach for managing malignancies that are resistant to systemic chemotherapy.[4] This TACE involves the selective administration of chemotherapeutic agents directly into the arterial blood supply of the tumor, combined with embolization to block the blood vessels feeding the tumor. This dual mechanism enhances the local delivery of chemotherapy, leading to higher intratumoral drug concentrations while simultaneously reducing the tumor's blood supply, thereby starving it of oxygen and nutrients.[5]

The embolization procedure cuts off tumor blood nutrition, attempting to provoke lesion ischemic, which acts synergistically with the chemotherapy cytotoxic effect, enhancing tumor necrosis.[6] This TACE has been most widely used in the treatment of hepatocellular carcinoma (HCC), where it has demonstrated significant improvements in local tumor control and overall survival in patients with intermediate-stage disease. Its success in HCC has led to growing interest in exploring its utility in other malignancies, including soft tissue sarcomas.[7]

A further advancement in the TACE technique is the use of drug-eluting beads (DEBs), which can absorb and slowly release chemotherapeutic agents over time, a method known as drug-eluting bead transarterial chemoembolization (DEB-TACE). The DEBs are microspheres that serve both as embolic agents to block the tumor's blood supply and as drug carriers to deliver high doses of chemotherapy directly to the tumor site.[8] The primary advantage of DEB-TACE is its ability to provide a controlled and sustained release of the chemotherapeutic agent, ensuring that the drug remains concentrated in the tumor tissue for an extended period. This reduces the systemic toxicity that is often associated with traditional chemotherapy, such as bone marrow suppression and gastrointestinal side effects.[9]

In liver cancer, particularly hepatocellular carcinoma, DEB-TACE has shown superior

efficacy and safety compared to conventional TACE. Studies have demonstrated that the sustained release of chemotherapy from DEBs leads to improved local control of the tumor and fewer systemic side effects, making it a preferred treatment option for patients with liver malignancies. However, the use of DEB-TACE in the treatment of soft tissue sarcomas is still in the early stages of investigation. Given the aggressive nature of many STS subtypes and their resistance to systemic chemotherapy, DEB-TACE offers a promising alternative by delivering targeted chemotherapy directly to the tumor, potentially improving treatment outcomes in patients with advanced disease. Neoadjuvant chemotherapy is commonly used in STS to shrink tumors before surgical resection, thereby facilitating complete removal and reducing the risk of recurrence. However, in cases where surgery is not an option, chemotherapy alone may not be sufficient to control the disease. DEB-TACE presents a potential solution, especially in patients with unresectable or metastatic STS, by offering a localized therapy that enhances the effects of chemotherapy while minimizing systemic exposure. The dual action of delivering high doses of chemotherapy directly to the tumor and simultaneously cutting off its blood supply makes DEB-TACE an attractive option for managing advanced STS, particularly in cases where other treatments have failed.[10]

This study aims to evaluate the efficacy and safety of DEB-TACE in the treatment of advanced soft tissue sarcomas. A retrospective analysis of 30 patients treated with DEB-TACE at Prof. Dr. R. D. Kandou Hospital, Manado, Indonesia, between 2020 and 2023, was conducted. The primary outcomes assessed include overall response rate (ORR) based on the modified Response Evaluation Criteria in Solid Tumors (mRECIST) and the incidence of treatment-related adverse reactions, such as post-embolization syndrome and bone marrow suppression. Secondary outcomes include overall survival (OS) and progression-free survival (PFS) in this patient cohort. By contributing to the growing body of evidence supporting the use of DEB-TACE, this study seeks to provide insights into the role of this novel therapy in managing advanced STS. Given the complexity of STS and the limitations of current treatment options, DEB-TACE offers a potentially valuable treatment modality that could improve patient outcomes and expand the therapeutic arsenal available for this challenging group of tumors. The findings of this study will help to clarify the clinical benefits and risks associated with DEB-TACE and may lay the groundwork for future prospective trials aimed at establishing this technique as a standard treatment option for advanced soft tissue sarcomas.

METHODS

A retrospective study was conducted to evaluate the efficacy and safety of drug-eluting bead transarterial chemoembolization (DEB-TACE) in patients with advanced soft tissue sarcomas (STS) treated at Prof. Dr. R. D. Kandou Hospital, Manado, Indonesia, between 2020 and 2023. Thirty patients diagnosed with advanced STS, either newly diagnosed or relapsed cases, were included in the study. All patients received DEB-TACE as the primary therapeutic intervention.

The therapeutic efficacy of DEB-TACE was evaluated using the modified Response Evaluation Criteria in Solid Tumors (mRECIST), which is used to assess tumor response to treatment. The overall response rate (ORR) was calculated based on the proportion of patients who achieved complete response (CR), partial response (PR), or stable disease (SD). Data on baseline characteristics, including age, gender, cancer status (new onset or relapsed), and Eastern Cooperative Oncology Group (ECOG) performance status, were collected.

Adverse reactions to the treatment were recorded, with a focus on post-embolization syndrome symptoms (fever, pain, nausea, vomiting) and grade II or higher bone marrow suppression. The morbidity and mortality rates associated with DEB-TACE were also documented. Statistical analysis was performed using SPSS 22.0 software, with a significance level of $p < 0.05$.

RESULTS

A total of 30 patients with advanced soft tissue sarcoma (STS) were treated with drug-eluting bead transarterial chemoembolization (DEB-TACE) between 2020 and 2023 at Prof. Dr. R.D.

Kandou Hospital, Manado. The demographic and baseline characteristics of the patients are outlined in Table 1. The mean age of the patients was 65.4 years (SD 20.6), with a male-to-female ratio of 17:13. Among the 30 patients, 28 were newly diagnosed cases, and two were cases of recurrent sarcoma. The performance status of the patients, measured using the ECOG score, showed that 20 patients had a score of 1, while 10 patients had a score of 2.

Table 1. Baseline characteristics of patients

Characteristics of patients	Number
Age (SD)	65.4 (20.6)
Gender (male: female)	17:13
Histological type	soft tissue sarcoma
Cancer status	
New onset	28
Relapsed	2
ECOG score	
1	20
2	10

The ORR evaluated using mRECIST criteria, was 76.7% ($p<0.05$), with five patients achieving complete response (CR), 18 achieving partial response (PR), and seven patients showing stable disease (SD) (Table 2). No patients experienced progressive disease during the study. The treatment-related adverse reactions included post-embolization syndrome, which manifested as fever (27%), pain (53.3%), and vomiting (36.6%) (Table 3). Additionally, grade II or higher bone marrow suppression occurred in 20% of patients. Despite these side effects, the overall morbidity rate was 93.3%, and no treatment-related mortality was observed (Table 4).

Table 2. Efficacy of DEB-TACE (%)

	Number	CR	PR	SD	ORR
Group	30	5	18	7	23

Table 3. Treatment related adverse reaction of DEB-TACE

Adverse reactions	Number (%)
Fever	8 (27)
Pain	16 (53.3)
Vomiting	11 (36.6)
Grade II or above bone marrow suppresion	6 (20)

Table 4. Mortality and morbidity related DEB-TACE

Items	Total Case (%)
Morbidity	28 (93.3)
Mortality	0

DISCUSSION

The results of this study demonstrate that DEB-TACE is a highly effective and relatively safe treatment modality for patients with advanced soft tissue sarcomas (STS). With an overall response rate of 76.7%, the therapeutic efficacy of DEB-TACE in this study was notable, particularly considering the advanced nature of the disease. The fact that five patients achieved

complete response (CR) and 18 achieved partial response (PR) underscores the potential of DEB-TACE to induce significant tumor shrinkage and improve local disease control. These findings align with previous studies on the use of DEB-TACE in liver malignancies, where it has been shown to provide superior local control compared to traditional systemic chemotherapy.[4]

One of the key advantages of DEB-TACE lies in its ability to deliver a high concentration of chemotherapeutic agents directly to the tumor site while minimizing systemic exposure. This targeted approach likely contributed to the favorable response rates observed in this study, as well as the relatively low incidence of severe systemic side effects. The drug-eluting beads used in DEB-TACE slowly release chemotherapy over an extended period, allowing for sustained tumor exposure to the drug and enhancing the overall therapeutic effect. Moreover, the embolization process helps to reduce the tumor's blood supply, creating a synergistic effect that further enhances tumor regression. Despite the promising results, the treatment was not without its challenges. Post-embolization syndrome (fever, pain, nausea, and vomiting) was observed in a significant proportion of patients, affecting up to 53.3% in terms of pain and 36.6% with vomiting. These symptoms are consistent with other studies on embolization therapies, as the blockage of blood flow to the tumor often results in local inflammation and ischemia, which can cause discomfort. However, these adverse reactions were generally manageable with supportive care, and no life-threatening complications were reported.[9]

The incidence of grade II or higher bone marrow suppression in 20% of patients is an important consideration, as it suggests that while DEB-TACE minimizes systemic toxicity, there is still a risk of hematologic side effects, likely due to some systemic absorption of the chemotherapy. However, the absence of treatment-related mortality and the overall safety profile of DEB-TACE in this study indicate that it is a feasible option for patients with advanced STS, particularly those who are not candidates for surgery. The high morbidity rate (93.3%) reflects the advanced stage of the disease and the intensive nature of the treatment. However, given the lack of treatment-related mortality, the morbidity can be considered an acceptable trade-off, especially considering the significant tumor response rates achieved with DEB-TACE. The ability of DEB-TACE to provide superior short-term treatment efficacy compared to traditional systemic chemotherapy offers hope for improving outcomes in patients with advanced STS, a population that has traditionally been difficult to treat.[9]

CONCLUSION

This study highlights the efficacy and safety of DEB-TACE as a treatment modality for advanced soft tissue sarcomas. With an ORR of 76.7% and a manageable safety profile, DEB-TACE presents a viable alternative for patients who are not candidates for surgical resection. Future studies are needed to further refine this treatment approach and explore its long-term outcomes, particularly in comparison to other available therapies for advanced STS.

Conflict of Interest

The authors affirm no conflict of interest in this study.

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