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ORIGINAL RESEARCH

Necessity of Prophylactic Anticoagulation Therapy Following Inferior Vena Cava Stent Placement in Patients with Cancer

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Abstract:

Purpose: Although percutaneous stent placement for malignant inferior vena cava syndrome is a highly feasible and effective treatment option, there is no clear evidence for the necessity of prophylactic anticoagulation therapy after inferior vena cava stent placement. This study retrospectively evaluated the necessity of prophylactic anticoagulation following inferior vena cava stent placement in patients with malignant inferior vena cava syndrome.

Methods: The data of 54 patients (28 men and 26 women; median age 61.2 years) with malignant inferior vena cava syndrome who received inferior vena cava stent placement between 2011 and 2021 were retrospectively reviewed. Prophylactic anticoagulation was administered to 15 of 54 patients (27.8%) following stent placement. Symptom recurrence rates at 1 and 2 months after stent placement were compared between patients with and without prophylactic anticoagulation using Gray relational analysis. The timeline of symptom recurrence, survival time, and adverse events were also evaluated.

Results: At 1 and 2 months, symptom recurrence rates were 48.6% and 71.4%, respectively, in patients with prophylactic anticoagulation and 28.3% and 37.0%, respectively, in patients without prophylactic anticoagulation. The overall median follow-up duration was 27 days and that of the patients with and without prophylactic anticoagulation was 37 and 25 days, respectively. The median survival times of patients with and without anticoagulation therapy were 69 and 30 days, respectively ($p = 0.236$). No procedure-related complications occurred.

Conclusions: There was no significant difference in the symptom recurrence rates after inferior vena cava stent placement with or without prophylactic anticoagulation in this study.

Keywords:
malignant inferior vena cava syndrome, inferior vena cava stent, anticoagulation therapy

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Introduction

Malignant obstruction of the inferior vena cava (IVC) may lead to the development of IVC syndrome (IVCS), with symptoms such as edema in the lower extremities, pelvis, genital organs, and skin; ascites and abdominal distension; and renal or hepatic dysfunction [1-3]. Conservative medical treatment, such as diuretics and albumin, or observation is often used for IVCS. However, IVCS significantly deteriorates patients' quality of life and may become refractory to medical treatments.

Several studies have demonstrated that percutaneous stent placement for IVCS is highly feasible and effective, with technical success rates of 97.7%-100% and clinical success rates of 60%-86.4% [1, 3-7]. Although there are some reports of anticoagulant therapy after IVC stent placement for benign IVC obstruction or stenosis [8, 9], the use of anticoagulants for malignant tumors is controversial, given the risk of bleeding in patients with advanced-stage cancer [10, 11]. Additionally, there is no clear evidence whether prophylactic anticoagulation is necessary after IVC stent placement in patients with malignant tumors.

We hypothesized that prophylactic anticoagulation following IVC stent placement for malignant IVCS is not essential; if this hypothesis is proven as correct, adverse bleeding events in patients with cancer can be prevented. The aim of this study was to evaluate the necessity of prophylactic anticoagulation following IVC stent placement for malignant

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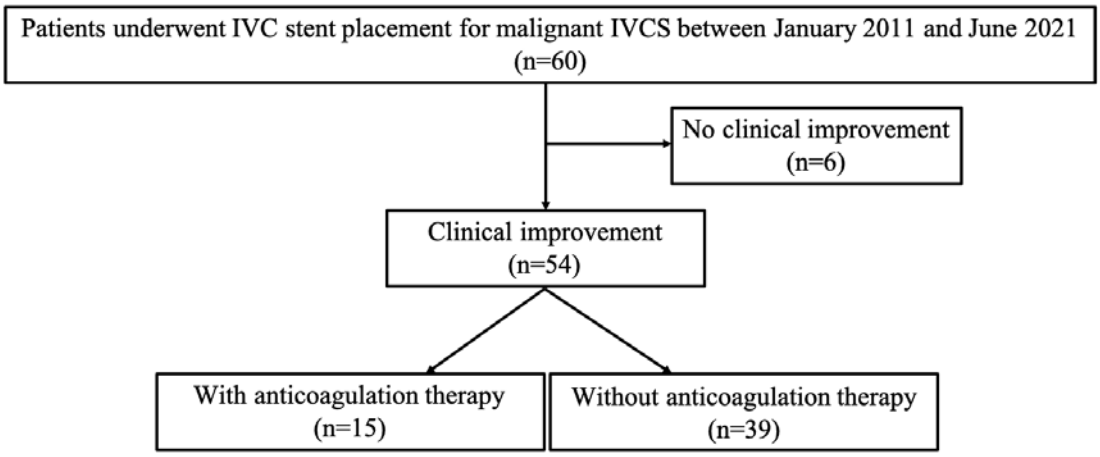

Figure 1. Flowchart describing study progression, from stent placement to symptomatology either with or without prophylactic anticoagulation treatment.

Table 1. Characteristics of Patients who Underwent Inferior Vena Cava Stent Placement between January 2011 and June 2021.

Variable		Anticoagulation (−)	Anticoagulation (+)
Number of patients		39	15
Age (years)		61.4 (30–90)	60.6 (16–81)
Sex		Male, 22; Female, 17	Male, 6; Female, 9
Etiology	Metastatic liver tumor	25 (64.1%)	10 (66.6%)
	Primary liver tumor	5 (12.8%)	1 (6.7%)
	Lymph node metastasis	6 (15.4%)	1 (6.7%)
	Other diagnoses (local recurrence or pleural dissemination of various malignant tumors)	3 (7.7%)	3 (20.0%)

IVCS.

Material and Methods

Study design

This was a single-institute, retrospective, descriptive study that assessed the safety and efficacy of prophylactic anticoagulation following IVC stent placement. This research has been approved by the Institutional Review Boards of the authors' affiliated institution. All patients provided written informed consent to undergo stent placement.

Patients

This study included patients who underwent stent placement for IVCS between January 2011 and June 2021. Considering that the aim of this study was to evaluate the necessity of prophylactic anticoagulation therapy, six patients without initial clinical improvement were excluded, which was defined as no improvement of clinical symptoms after stent placement even if stent placement was successfully performed. Fifty-four patients (28 men and 26 women) with a median age of 61.2 years (range: 16-90 years) were included. Anticoagulation therapy was administered to 15 patients due to physicians' choice because there was no fixed protocol for anticoagulation therapy (**Fig. 1**). There were no patients receiving antiplatelet before and after stent placement. The most frequent etiology of IVCS was metastatic liver tumor. Additional patient characteristics are shown in **Table 1**.

Stent placement procedure

All procedures were performed under local anesthesia with mild intravenous analgesics. The IVC stent placement technique has been described in detail elsewhere [12]. After confirming the stenotic area of the IVC using digital subtraction venography, a 0.035-inch hydrophilic guidewire (Radifocus Guidewire M; Terumo, Tokyo, Japan) was traversed and a self-expandable metallic bare stent (Spiral Relief; COSMOTEC, Tokyo, Japan, or Spiral Z; Medico's Hirata, Osaka, Japan) of 16- to 20-mm width and 60- to 100-mm length was placed. The stent was placed in the intrahepatic and extrahepatic vena cava in 43 and 11 cases, respectively. The procedure was completed after confirming the disappearance of IVC stenosis and a reduction in collateral vessels. Preballoon or postballoon dilatation was performed when stent delivery was impossible or when the angiographic findings did not sufficiently improve following

Table 2. Details of Stent Placement Procedures.

Variable		Anticoagulation (−)	Anticoagulation (+)
Length of stenosis (cm)		8.7 (3–24)	8.3 (4–19)
Number of stents		1.7 (1–4)	1.9 (1–3)
Type of stent	Spiral Relief (COSMOTEC, Tokyo, Japan)	5 (12.8%)	6 (40.0%)
	Spiral Z (Medico's Hirata, Osaka, Japan)	34 (87.2%)	9 (60.0%)
Procedure time (min)		60.9 (20–150)	66.7 (30–120)

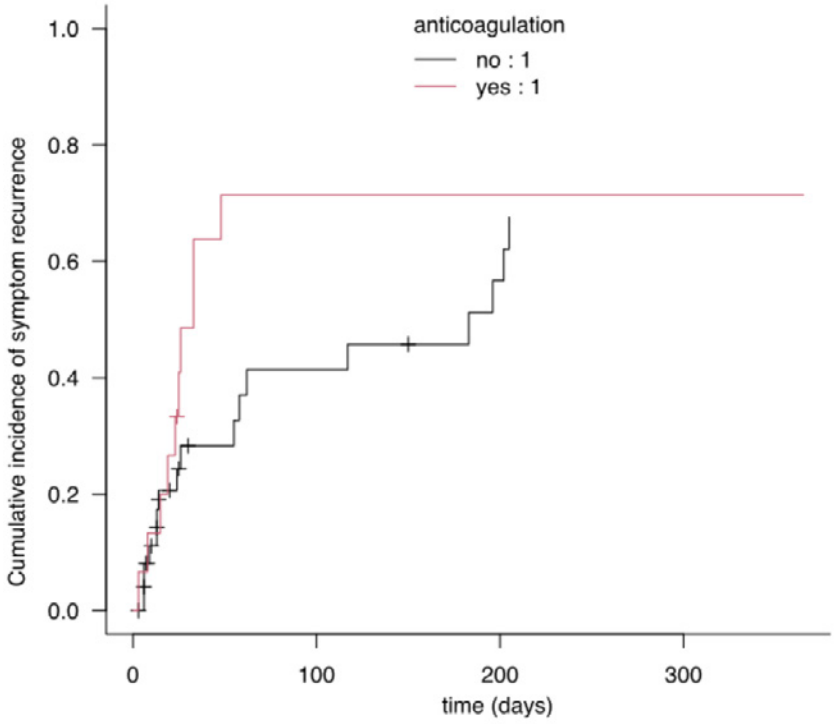

Figure 2. Graph depicting the cumulative incidence of symptom exacerbation in patients, with death as a competing risk. The black line represents patients who did not receive anticoagulation treatment, and the red line represents patients who received anticoagulation treatment following stent placement.

stent placement. Procedural details are presented in **Table 2**.

Outcome measures

The primary outcome measure was the difference in the clinical efficacy of IVC stents between patients with and without prophylactic anticoagulation; these outcomes were determined by evaluating the symptom recurrence rates at 1 and 2 months after stent placement. The timeline of symptom recurrence, survival time, and adverse events were also evaluated. Additionally, for patients with imaging follow-up, the median follow-up time and stent patency were evaluated. Adverse events were categorized on the basis of the classification system established by the Society of Interventional Radiology [13]. All clinical events were extracted through a chart review.

Statistical analysis

Statistical analyses were performed using the R software package (R Foundation, Vienna, Austria). Symptom recurrence rates were calculated using Gray relational analysis, in which the patient's death before symptom recurrence was considered a competing risk (**Fig. 2**). Symptom recurrence rates at 1 and 2 months after stent placement were compared between patients with and without prophylactic anticoagulation therapy. The survival analysis was calculated using the Kaplan-Meier method. Statistical significance was determined by a p value of <0.05.

Results

Follow-up and survival times

The overall median follow-up duration was 27 days (range: 2-1295 days) and that of the patients with and without prophylactic anticoagulation was 37 days (range: 11-1295 days) and 25 days (range, 2-430 days), respectively. The median survival times of patients with and without anticoagulation therapy were 69 days (95% confidence interval

[CI]: 24-168) and 30 days (95% CI: 22-150), respectively (p = 0.236). Imaging follow-up was performed in 25 cases (23 contrast-enhanced CT and 2 digital subtraction venography), including all cases of patients with prophylactic anticoagulation and 10 of 39 cases of patients without prophylactic anticoagulation (median follow-up times were 32.5 and 35 days, respectively). Additionally, stent patency was confirmed in 24 of 25 cases (96%). Anticoagulation therapy was not administered in a patient with stent occlusion.

Symptom recurrence

At 1 and 2 months, symptom recurrence rates were 48.6% (95% CI: 20.3-72.1) and 71.4% (95% CI: 36.4-89.4), respectively, in patients with prophylactic anticoagulation and 28.3% (95% CI: 13.6-45.0) and 37.0% (95% CI: 19.3-54.9), respectively, in patients without prophylactic anticoagulation. No significant differences were observed between the groups. Furthermore, no significant differences were observed in the median time to symptom recurrence (with anticoagulants, 33 days; without anticoagulants, 183 days; p = 0.393).

Complications

No minor or major procedure-related complications occurred. No bleeding events occurred during the follow-up period.

Discussion

Our results suggest that there is no significant difference in the symptom recurrence rates at 1 and 2 months after IVC stent placement with or without prophylactic anticoagulation therapy (48.6% and 71.4% with prophylactic anticoagulation therapy vs 28.3% and 37.0% without prophylactic anticoagulation therapy).

At present, there is no consensus on the administration of prophylactic anticoagulants after IVC stent placement for both benign and malignant etiologies. Some reports have described the necessity of prophylactic anticoagulation after IVC stent placement. Brountzos et al. reported that 33% of patients who received IVC stent placement for malignant IVCS without anticoagulation therapy presented with symptom recurrence during the mean follow-up period of 62 days (range: 1-932 days) [1]. The reason not to administer anticoagulation therapy was because the cohort primarily comprised patients with advanced liver tumors and impaired liver function; these patients were inherently more at risk of bleeding.

In patients with benign IVCS, the efficacy of anticoagulation remains controversial, as in the patients with malignant tumor. Endo et al. reported that concomitant antiplatelet and anticoagulation therapy improved iliocaval venous stent patency compared with anticoagulation therapy alone [8]. Ali et al. suggested that permanent anticoagulation therapy was not needed after stent placement for chronic venous obstruction; however, antiplatelet therapy was suitable for stent maintenance, particularly in nonthrombotic cases [9]. On the contrary, a recent retrospective observational cohort study reported that there was no difference between patient groups receiving subtherapeutic and therapeutic anticoagulation in terms of procedure-related complication rates, rates of reintervention, and clinical improvement after nonthrombotic venous stent placement [14].

Bleeding should be avoided as much as possible in patients with cancer who are prone to coagulation abnormalities. Bleeding occurs in approximately 10% of patients with solid tumors [15] and may be fatal [16]. Considering this, it may be beneficial for patients with cancer to undergo IVC stent placement without unnecessary anticoagulation therapies if it can be proven that prophylactic anticoagulation is not needed in selected situations.

There are several limitations to this study. First, this was a retrospective study conducted at a single institution. Second, the sample size was small to achieve clear statistical significance. Although the results show that the group with prophylactic anticoagulation had nearly double the rate of exacerbation of symptom rates compared with the group without prophylactic anticoagulation, it is difficult to explain why these results were obtained due to the small number of cases. Third, the follow-up period was insufficient; however, an adequate follow-up period is uncertain, given the limited survival time of patients with malignant IVCS. Takeuchi et al. reported that the median survival time of patients who underwent IVC stent placement for malignant IVCS was as short as 67 days [4]. Additionally, follow-up tended to be difficult, as most patients were shifted to outpatient home care soon after stent placement. Fourth, in patients with anticoagulation, the timing and reason for the administration of anticoagulation and its protocol are not fixed. Furthermore, as multiple factors may affect lower-limb edema and ascites in patients with advanced-stage cancer, symptom recurrence does not always indicate obstruction of the IVC stent. Thus, prospective studies with risk stratification for stent occlusion and bleeding should explore potential indications for the use of prophylactic anticoagulants.

In conclusion, no significant difference was observed in the symptom recurrence rates after IVC stent placement with or without anticoagulation therapy in this study. However, further prospective studies with a larger sample size are warranted to determine the need for prophylactic anticoagulation therapy after IVC stent placement.

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Conflict of Interest: None

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tion, drafted the manuscript or revised it critically for important intellectual content, approved the final version of the manuscript to be published, and agreed to be accountable for all aspects of the work.

IRB: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required. This retrospective study was approved by the Institutional Ethics Committee (approval number: NCCH-2018-049).

Informed Consent: This study has obtained IRB approval (approval number: NCCH-2018-049) from the Institutional Ethics Committee, and the need for informed consent was waived. All patients provided written informed consent to undergo the procedure.

Consent for Publication: For this type of study, consent for publication is not required.

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