



## Research Paper

# Outcomes in patients managed with endovascular stent for malignant superior vena cava syndrome

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## ABSTRACT

**Background:** Malignant Superior Vena Cava Syndrome (SVCS) corresponds to the clinical manifestations due to the restriction of venous return to the right atrium secondary to obstruction of the superior vena cava and/or its main tributaries for a tumor. Endovascular management has proven to be safe, effective and cause a fast symptomatic relief in patients with SVCS. There is limited evidence in factors associated with outcomes in malignant setting for this procedure.

**Materials and methods:** An analytical retrospective study was conducted and included patients that underwent endovascular management for malignant SVCS at the National Cancer Institute of Colombia between May 2016 and May 2021. Clinical and technical variables were analyzed to find associations with outcomes in these patients.

**Results:** 54 patients were analyzed. Successful procedure rate was 94.4 %. At 10 months, the OS of the entire cohort of patients was 25 %. Patients with breast or lung cancer ( $P = 0.031$ ), unsuccessful procedure ( $P = 0.011$ ), and also with short time of symptoms to the date of the endovascular procedure ( $P = 0.027$ ) had worse OS. Multivariate analysis showed that lung cancer [HR = 2.55, 95%IC:(1.21–5.36)] and left internal jugular vein or left Innominate vein distal stent attachment [HR = 3.27, 95%IC:(1.31–8.15)] were independent factors for worst OS.

**Conclusions:** Based in the high success rate of the endovascular management and the better outcome in patients with early and successful procedure, this procedure should be considered as part of the multimodal treatment in patients with SVCS independent of the clinical scenario and the oncological diagnosis.

## Introduction

Superior Vena Cava Syndrome (SVCS) corresponds to the clinical manifestations due to the restriction of venous return to the right atrium secondary to obstruction of the superior vena cava (SVC) and/or its main tributaries [1,2]. Different etiologies have been described, but the malignant cause is the most frequent with 60–90 % of cases [3]. Additionally, 2–4 % of patients with lung cancer will develop SVCS at some point in the course of their disease [3]. SVCS can occur by single or combined mechanisms: tumor external venous compression, tumor invasion and/or intraluminal thrombosis. The clinical severity worsens if the level of obstruction is below or at the insertion of azygos vein into the SVC, because this is the main collateral pathway for venous return to

the right atrium [4]. The symptoms may onset acutely or sub-acutely depending on the degree of obstruction and its cause. For a long time, SVCS was considered an oncologic emergency, however, nowadays it is more frequent to have a progressive presentation that can develop over 2 to 4 weeks [3].

The clinical scenario is determined by the Kishi severity scale that includes neurological, facial, laryngeal and cardiovascular signs and symptoms. A score >4 reflects severity and an indication for percutaneous stenting to reduce venous pressure and prevent cerebral edema [4]. Although the treatment of SVCS is initially aimed at symptomatic management, the specific treatment depends on the start of systemic chemotherapy and/or radiotherapy according to the underlying etiology, however, the response to these therapies usually occurs within 2 to

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3 weeks [3].

Radiotherapy remains an important tool in the management of patients with SVCS. In the last decade, the use of hypofractionated radiotherapy and stereotactic body radiotherapy has been considered for patients with SVCS and lung cancer, obtaining equivalent results and toxicity to conventional radiotherapy, decreasing costs, exposure and increasing the tolerance in patients with SVCS [5,6]. In 1984, Ahmann [7] described normal SVC flow by venography in 11 % of patients after radiotherapy, persistent SVC obstruction in 24.2 % and a clinical response rate of 50 to 70 %. Since 1986, when Charnsangavej et al. described the use of stents for the management of SVCS [8], different series have been reported greater and faster symptomatic relief (6–24 h) with endovascular management. Success rates of 95–97 % and a rapid resolution of symptoms, make endovascular stenting an unquestionable procedure [9,10], however, it has been difficult to demonstrate a survival benefit due to the variability of the underlying pathologies and the short overall survival time (3–6 months) [10,11].

Despite the satisfactory results of endovascular management in patients with SVCS, there is limited evidence in malignant setting. The aim of this study was to describe the outcomes in patients with SVCS for solid tumors managed with endovascular stents and their associations with clinical factors, characteristics of the obstruction and technical aspects of the procedure. We hypothesized that the Kishi clinical severity scale score for SVCS and overall survival in these group of patients are related variables.

## Materials and methods

An analytical retrospective study was conducted and included patients older than 18 years that underwent endovascular management for SVCS secondary to solid tumors with confirmed malignant histology at the National Cancer Institute (INC) of Colombia between May 2016 and May 2021. Medical records were reviewed and RedCap® 7.1.2 platform was used to collect demographic, clinical, radiological, therapeutic characteristics, and outcomes.

All patients with clinical suspicion of SVCS were evaluated with tomography to confirm the diagnosis and measure the size of the veins. The decision for endovascular treatment in each case was made by the treating oncologic group and the INC emergency team. The type of stent used was the 14 mm diameter uncovered self-expandable stent of Cordis S.M.A.R.T® CONTROL™ Nitinol Stent System, after dilatation with a 12–14 mm angioplasty balloon. The access site was the right common femoral vein in most cases. The right jugular access was used, in case the femoral approach was not possible.

Overall survival (OS) was defined as the time from the date on which the SVC stenting procedure was performed until the patient's death or the last day of follow-up. Recurrence was defined as the onset of symptoms compatible with SVCS with imaging confirmation (tomography or cavography) after the endovascular stenting procedure. Recurrence free survival (RFS) was defined as the time between SVC stenting and the recurrence of a new episode of SVCS if there was it.

The Kishi severity scale was calculated retrospectively according to the symptoms reported in the patients' medical records. This severity scale is based on the type of signs and symptoms presented by the patient prior to the endovascular procedure and its maximum score is 10. In each system the score could be zero or the highest value according to the symptoms. Neurological symptoms add 4 points when the patient presents stupor, coma or blackout; three points for blurry vision, headache, dizziness, or amnesia; two points for changes in mentation or one for uneasiness. Respiratory symptoms add 3 points for orthopnea or laryngeal edema; two for stridor, hoarseness, dysphagia, glossal edema, or shortness of breath and one for cough or pleural effusion. Facial signs or symptoms add 2 points for lip edema, nasal stiffness, or epistaxis or one for facial swelling. Venous dilation includes neck or arm veins distention, upper extremity swelling, or upper body plethora [4], Table 1.

Stanford classification is an anatomical classification according to

**Table 1**

Kishi scoring system for clinical severity of superior Vena Cava Syndrome.

Signs and symptoms	Score
Neurologic symptoms	
Stupor, coma, or blackout	4
Blurry vision, headache, dizziness, or amnesia	3
Changes in mentation	2
Uneasiness	1
Laryngopharyngeal or thoracic symptoms	
Orthopnea or laryngeal edema	3
Stridor, hoarseness, dysphagia, glossal edema, or shortness of breath	2
Cough or pleural effusion	1
Nasal an facial signs or symptoms	
Lip edema, nasal stiffness, epistaxis, or rhinorrhea	2
Facial swelling	1
Venous dilatation	
Neck vein or arm vein distention, upper extremity swelling, or upper body plethora	1

the degree of obstruction and the activation and permeability of the azygos system. Type I is a partial obstruction (<90 %) of the SVC with patency and antegrade flow in the azygos vein. Type II is almost complete obstruction (90–100 %) of the SVC with patency and antegrade flow in the azygos vein. Type III is a complete SVC obstruction with retrograde flow in the azygos vein, but without involvement of the mammary and epigastric veins, and Type IV is a complete obstruction of the SVC and the azygos system with development of collaterals in the chest wall and internal mammary vein [12].

Successful procedure was determined when permeability of the SVC was obtained with resolution of the obstruction and decrease in collateral flow visualized in the cavography at the end of the endovascular stenting procedure.

All the information collected from the medical records and registered in RedCap® was verified by monitor of clinical investigation from the INC.

Numerical variables were presented in medians and interquartile ranges (IQR), while the categorical variables were presented in absolute values and percentages. In the first instance, the assumption of normality was validated for quantitative variables using the Shapiro Wilk test. To evaluate whether statistically significant differences exist, the Wilcoxon signed-rank test or *t*-test was used in the case of quantitative variables and Fisher's exact test or the Freeman Halton test in the case of qualitative variables. Kaplan-Meier curves and the log-rank test were used to analyze the OS and RFS patients with SVCS in different subgroups. All statistical analyses were performed with the R - Project v4.1.1 software.

The ethics committee at our institution approved the protocol before collecting patient's data from clinical records (N° CEI-00643-21) and supervised by an independent clinical monitoring group.

## Results

In this study, 54 patients were included. 31 (57.4 %) were men. The mean age was  $56.1 \pm 14.7$  years. The most frequent cause of SVCS was lung cancer ( $n = 21$ , 38.9 %) followed by breast cancer ( $n = 10$ , 18.5 %), Table 2. The median time from the onset of symptoms of SVCS to the endovascular procedure was 20 days (IQR: 27.0). 7.4 % of patients had a previous episode of SVCS (none of these patients had more than one previous episode), these patients were managed with.

Additionally, 85.2 % of the cases had facial symptoms; 90.7 % ( $n = 49$ ) had respiratory symptoms, of these 61.2 % ( $n = 30$ ) experienced stridor, hoarseness, dysphagia or shortness of breath; 14.8 % ( $n = 8$ ) had neurological symptoms; venous dilatation was described in 64.8 % ( $n =$

**Table 2**  
Demographic, clinical and technical characteristics of patients with Superior Vena Cava Syndrome (SVCS) undergoing endovascular management.

Variable		Total (N = 54)
Age (years)	Mean ± SD <sup>a</sup>	56.1 ± 14.7
Gender, n (%)	Male	31 (57.4)
	Female	23 (42.6)
Oncologic diagnosis, n (%)	Lung cancer	21 (38.9)
	Breast cancer	10 (18.5)
	Neuroendocrine tumor	6 (11.1)
	Germ cell tumor	5 (9.3)
	Thymus neoplasms	3 (5.6)
	Primary unknown	3 (5.6)
	Thyroid cancer	2 (3.7)
	Other <sup>b</sup>	4 (7.4)
Facial symptoms, n (%)	Yes	46 (85.2)
	No	8 (14.8)
Respiratory symptoms, n (%)	Yes	49 (90.7)
	No	5 (9.30)
Neurological symptoms, n (%)	Yes	8 (14.8)
	No	46 (85.2)
Venous dilatation, n (%)	Yes	35 (64.8)
	No	19 (35.2)
Kishi severity score, n (%)	2	14 (25.9)
	3–4	33 (61.1)
	5–6	7 (13.0)
Stanford classification, n (%)	I	3 (5.6)
	II	6 (11.1)
	III	16 (29.6)
	IV	29 (53.7)
Presence of thrombosis on pre-procedure imaging, n (%)	Yes	14 (25.9)
	No	40 (74.1)
Level of obstruction in the superior vena cava, n (%)	Superior vena cava + right and left innominate vein	30 (55.6)
	Superior Vena Cava	12 (22.2)
	Superior Vena Cava + right innominate vein	10 (18.5)
	Superior Vena Cava + left innominate vein	2 (3.70)
Number of stents placed during the procedure, n (%)	0	1 (1.9)
	1	13 (24.1)
	2	25 (46.3)
	3	13 (24.1)
	4	2 (3.7)
Stents distal attachment site, n (%)	Right jugular vein	24 (44.4)
	Right innominate vein	16 (29.6)
	Left innominate vein	6 (11.1)
	Superior Vena Cava	5 (9.3)
	Left jugular vein	2 (3.7)
	Other	1 (1.9)

<sup>a</sup> SD: standard deviation.

<sup>b</sup> Other: includes cervical cancer, colon cancer, prostate cancer and mesothelioma.

35). The median Kishi score for the entire series was 3.0 (IQR: 1.75); meanwhile, for patients with germ cell and thymus tumors was 4.0 (IQR: 0.00). Description of the findings of the Kishi score and Stanford classification are summarized in Table 2.

In this series, anticoagulation treatment was used in 16.7 % of patients and this management was related to the presence of thrombosis in imaging studies prior to endovascular treatment. Furthermore, the steroids were used as an initial treatment in 61.1 % before the endovascular management. Chemotherapy and radiotherapy prior to endovascular management was used in 16.7 % and 54 %, respectively. 37 % of patients received chemotherapy or radiotherapy after endovascular procedure.

Successful procedure was performed in ( $n = 51$ ) 94.4 % of patients. The level of obstruction was mostly in the superior vena cava and bilateral innominate veins ( $n = 30$ , 55.6 %). 25.9 % ( $n = 14$ ) of patients presented thrombosis prior to the procedure; the median percentage of obstruction in the superior vena cava was 95 % (IQR: 5.00) during the

endovascular procedure. The number of stents placed most frequently was 2 ( $n = 25$ , 46.3 %); the most frequent distal stent attachment site was the right jugular vein ( $n = 24$ , 44.4 %), followed by the right innominate vein ( $n = 16$ , 29.6 %), Table 2.

The median follow-up period was 14.3 months. Of the 54 patients, 2 (3.7 %) patients had recurrence following the endovascular procedure, with a median RFS of 18.0 months (IQR: 17.8). Finally, 81.5 % of patients died during follow-up, with a median survival of 2.4 months [CI95%:1.28–4.80]. At 10 months, the OS of the entire cohort of patients was 25 % [CI95%:15.5–40.4], (Fig. 1A) Table 3.

Additionally, patients with lung cancer as the etiology of SVCS ( $P = 0.002$ ) and with a short time of symptoms to the date of the endovascular procedure ( $P = 0.027$ ) had worse survival, Table 4.

Kaplan-Meier curves showed that patients with breast or lung cancer ( $P = 0.031$ ), unsuccessful procedure ( $P = 0.011$ ), and a distal stent attachment in left Internal Jugular vein or left Innominate vein had worse OS (Fig. 1B, C and D). Meanwhile, there were no associations between survival and Kishi score ( $P = 0.097$ ), venous distension ( $P = 0.072$ ) and use of >2 stents ( $P = 0.079$ ), Fig. 2. Multivariate analysis showed that lung cancer diagnosis [HR = 2.55, 95%CI:(1.21–5.36),  $P = 0.014$ ] and left Internal jugular vein or left Innominate vein distal stent attachment site [HR = 3.27, 95%CI:(1.31–8.15),  $P = 0.011$ ] (HR = 3.01) were independent factors for worst overall survival, Table 5.

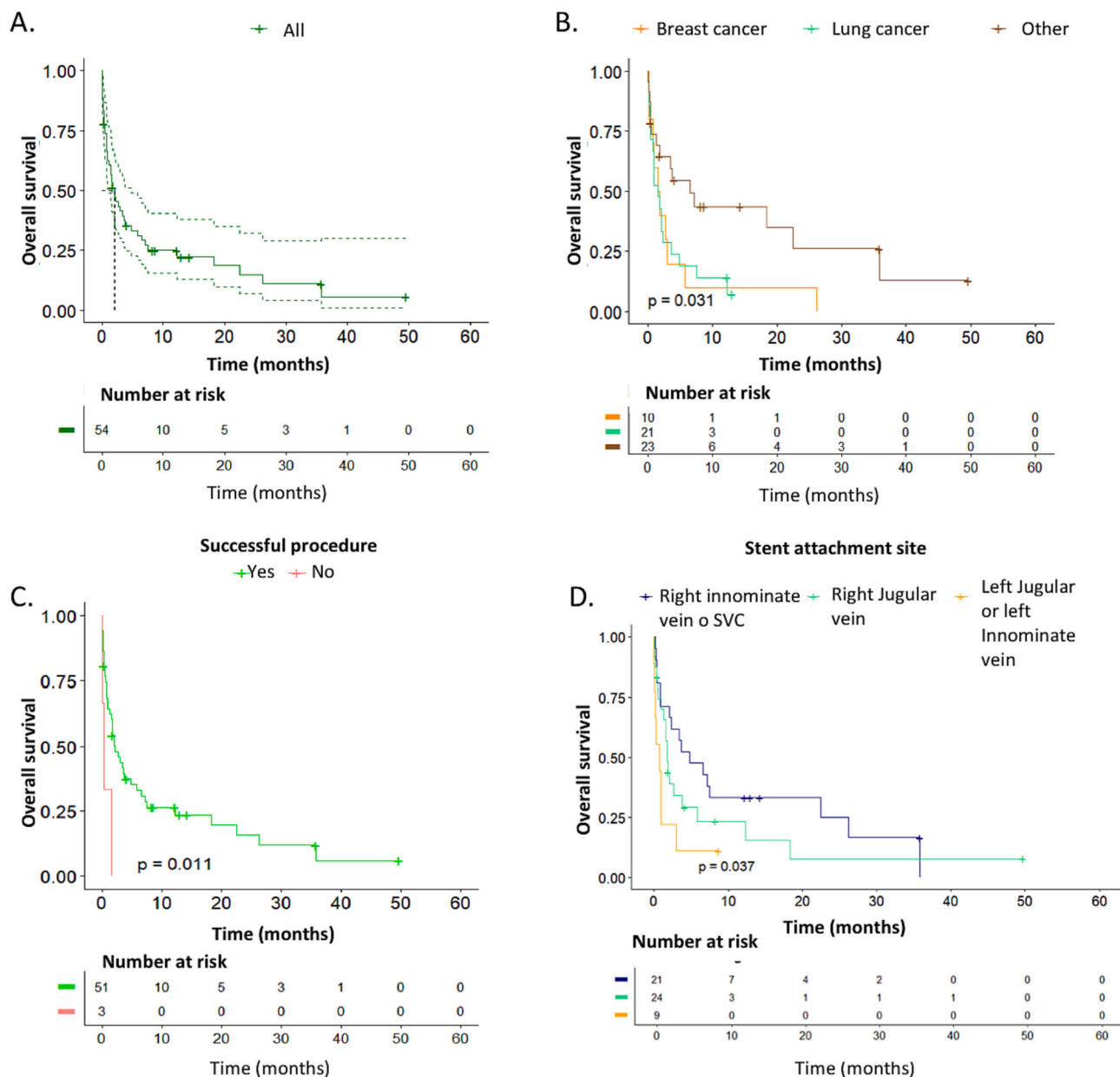
## Discussion

Malignant etiology is the most common cause of SVCS and includes hematologic malignancies and solid tumors [11,13]. SVCS due to hematologic malignancies has an excellent response to chemotherapy, being the main and first management in this scenario. However, for solid tumors, the time and variability of response to conventional specific therapies have led to a search for management with shorter response times and better success rates. Recently, endovascular therapy with stents has become the first-line treatment for the vast majority of patients with SVCS due to solid malignancies [10,11,14], although, consensus guidelines are lacking.

Although lung cancer has been described as the main cause of SCVS due to solid tumors, other etiologies have also been described, such as thymoma, primary germ cell neoplasms, mesothelioma, and mediastinal lymph node metastases from other neoplasms such as breast cancer [4,14,15] Rice and cols, described that bronchogenic carcinoma accounted for 46 % of the etiology of SVCS [13]. In our series lung cancer accounted for 38.9 % of cases that underwent endovascular stenting. Furthermore, we found an association between patients with lung or breast cancer and worse survival. These findings have been reported in other publications [11,16] despite major advances in multimodal therapies for these pathologies.

Although SVCS has been considered an oncological emergency, the clinical presentation of SVCS may take weeks or months, interestingly we found an association between the acute onset of symptoms and the mortality in patients, these findings can be explained because with a progressive and slow presentation the patient has the possibility of developing physiological adaptation mechanisms (venous dilatation, collateral circulation), which lead to an improved tolerance of the occlusion and a better response to endovascular management. The time of this process is reflected in some findings of the patient's physical examination, such as venous dilatation, and its severity in some imaging findings, such as the degree and level of venous obstruction [3]. Corresponding with these facts, we found that respiratory manifestations were the most common symptoms (90.7 %), followed by facial (85.2 %), and venous dilatation (64.8 %). These presentations vary from other reports which describes lower frequency of respiratory symptoms and collateral circulation [3,4,7]. Symptoms like stridor (laryngeal edema) or neurologic manifestations were less frequent, and they represented more severe cases and defined the urgency of an intervention.

Kishi scoring system was developed to assist the decision to



**Fig. 1.** Overall survival, Kaplan-Meier estimates: A) Entire cohort of patients. Stratified by: B) Oncological diagnosis C) endovascular procedure success D) Stent distal attachment site. Superior vena cava (SVC).

**Table 3**  
Survival of patients diagnosed with malignant Superior Vena Cava Syndrome (SVCS) taken to endovascular management.

	10 months- overall survival [IC95%]	p-Value	Mean survival (months)
All	25.0 [15.5–40.4]	–	2.04
Oncologic diagnosis			
Lung cancer	14.3 [5.01–40.7]	<b>0.031</b>	1.51
Breast cancer	10.0 [1.56–64.2]		1.66
Other	43.6 [26.6–71.5]		6.54
Kishi severity score			
2	21.4 [7.86–58.4]	0.097	1.05
3–4	31.3 [18.6–52.7]		2.92
5–6	NE <sup>a</sup>		0.75
Venous dilatation			
Yes	30.3 [17.8–51.4]	0.072	3.39
No	15.8 [5.59–44.6]		1.51

<sup>a</sup> NE: Not estimated.

endovascular management, initially a score of 4 or higher indicated a need for stenting [4]; However, with the high success rate of the endovascular procedure, this decision is currently based on the clinical scenario and oncological diagnosis. In our series, we did not find an association between Kishi score and survival, even in patients with 5–6 scores.

Therefore, these results could support the recommendation of endovascular treatment as part of the multidisciplinary management of SVCS patients with solid tumors regardless of the clinical severity score, in order to achieve a greater benefit in terms of symptom improvement.

Chemoradiation has been found to have a good outcome in patients with SVCS due to epithelial tumors, as it allows for maximal tumor response [16], with a maximal symptom improvement (80 %) in patients with small-cell lung cancer. However, this response takes between 2 and 4 weeks [4,17] and these conventional therapies are associated with numerous side effects and low response rates in certain tumors [14]. Furthermore, local edema caused by radiation may exacerbate



**Table 4**

Demographic and clinical characteristics of patients taken to endovascular management for Superior Vena Cava Syndrome (SVCS), according to mortality status.

Variable		Total (N = 54)	Death (n = 44)	Live (n = 10)	p-Value
Age, (years)	Mean ± SD*	56.1 ± 14.7	57.1 ± 14.7	52.0 ± 14.6	0.328
Oncological diagnosis, n (%)	Lung cancer	21 (38.9)	19 (43.2)	2 (20.0)	0.002
	Breast cancer	10 (18.5)	10 (22.7)	0 (0.0)	
	Neuroendocrine tumor	5 (9.3)	3 (6.8)	2 (20.0)	
	Germ cell tumor	10 (18.5)	8 (18.2)	2 (20.0)	
	Thymic neoplasms	3 (5.6)	3 (6.8)	0 (0.0)	
Onset of symptoms of SVCS (days)	Primary unknown	2 (3.7)	1 (2.3)	1 (10.0)	0.027
	Other	3 (5.6)	0 (0.0)	3 (30.0)	
Venous dilatation, n (%)	Mean [IQR**]	20.0 [27.0]	15 [23.0]	47.5 [61.2]	0.079
	Yes	35 (64.8)	26 (59.1)	9 (90.0)	
Kishi severity score	No	19 (35.2)	18 (40.9)	1 (10.0)	0.188
	Mean [IQR]	3.00 [1.75]	3.00 [2.0]	4.00 [0.75]	
Kishi severity score, n (%)	2	14 (25.9)	12 (27.3)	2 (20.0)	0.889
	3–4	33 (61.1)	26 (59.1)	7 (70.0)	
	5–6	7 (13.0)	6 (13.6)	1 (10.0)	

\*SD: Standard deviation.

\*\*IQR: Interquartile range.

\*\*\*Other: includes cervical cancer, colon cancer, prostate cancer and mesothelioma.

symptoms in the emergency scenario [17] and by itself may cause SVCS in the long term due to fibrosis [18]. In our patients, 16.6 % before and 37 % after stent placement received multimodal treatment with chemotherapy and radiotherapy, but these therapies were not related with survival.

Anticoagulation is another therapy frequently prescribed prior or after stent placement due to its highly thrombogenic effect during the first month. However, its efficacy has never been demonstrated [11,19] and, in this series, we did not find an association with the outcomes and this therapy.

We reported a technical success rate of 94.4 %, being similar to other reports (95–96.4 %) [20,21], additionally this success was associated

with a better survival in our series. Considering there is no standard treatment for SVCS, it is important to highlight the advantages of successful stenting on overall survival.

The number of stents required to achieve technical success is variable and seems to be related to patient prognosis [10,11]. Even though, we found a trend towards better survival in patients who needed <2 stents to resolve the obstruction, with a median survival of 2.63 vs. 0.92 months, this difference was not statistically significant (p = 0.079). To our knowledge, this is the first report who found an association between the distal stent attachment site and survival, being longer for patients with a distal attachment in the SVC or in the right innominate vein, in contrast with those with an attachment in the right jugular, left jugular or left innominate veins (p = 0.037), this finding could be explained for a longer and more severe obstruction, as well as less possibility of collateral circulation.

**Table 5**

Univariate and multivariate analysis of overall survival.

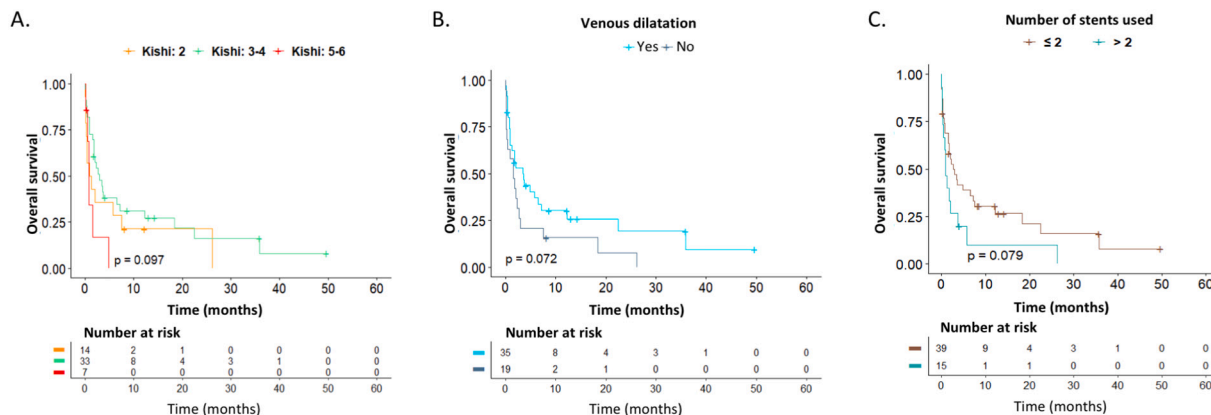
Variable	Univariate		Multivariate	
	HR* [CI**95%]	p-Value	HR [CI95%]	p-Value
Diagnostic				
Other	Ref.		Ref.	
Breast cancer	2.35 [1.04–5.34]	0.041	2.28 [0.95–5.46]	0.064
Lung cancer	2.37 [1.16–4.84]	0.018	2.55 [1.21–5.36]	0.014
Stent fixation				
SVC or right innominate vein	Ref.		Ref.	
Right jugular vein	1.47 [0.75–2.86]	0.300	1.73 [0.84–3.57]	0.140
Left jugular vein or left innominate vein	3.01 [1.26–7.18]	0.013	3.27 [1.31–8.15]	0.011
Number of stents used				
≤2	Ref.		Ref.	
>2	1.78 [0.93–3.40]	0.083	1.59 [0.79–3.18]	0.200
Recurrence of the SVCS****				
No	Ref.		Ref.	
Yes	0.45 [0.06–3.32]	0.400	1.10 [0.14–9.03]	0.900
Neurologic symptoms				
No	Ref.		Ref.	
Yes	1.54 [0.71–3.34]	0.300	2.20 [0.94–5.13]	0.068

\*HR: Hazard Ratio.

\*\*CI: confidence interval.

\*\*\*SVC: superior vena cava.

\*\*\*\*SVCS: superior vena cava syndrome.



**Fig. 2.** Overall survival, Kaplan-Meier estimates: A) Kishi severity score. B) Venous dilatation C) Number of stents used.

This series reports one of the highest overall survival rates in patients with SVCS (25 % at 10 months), almost five times higher than other data that report 2–5 % survival at 12 months [21–23]. With the current evidence, despite the short survival and poor prognosis of patients with SVCS, this pathology requires an effective and fast treatment. We consider percutaneous stent placement is a justified procedure, regardless of the life expectancy, due to the high success rate and faster relief of clinical symptoms reported in the literature [9–11].

Limitations of this study include its retrospective nature and small number of patients. But it shows the experience of the endovascular stent in the management of patients with SVCS in a cancer center in South America.

## Conclusions

Patients with SVCS for lung or breast cancer had a worse survival, despite the advances in multimodal therapy for these pathologies. The lack of association between Kishi score and survival, and the better outcome in patients with an early and successful endovascular procedure reported in these series, should be taken in count to include this procedure as part of the treatment in patients with SVCS. Patients with a distal stent attachment in the SVC or in the right innominate vein had better survival compared with those with an attachment in the right jugular, left jugular or left innominate veins, these findings should be considered in the previous evaluation of the obstruction extension and during the stent placement.

## Author contributions

Silvia Guerrero contributed in collection, analysis and interpretation of data, and writing of the manuscript. Julian Beltrán contributed in study design, analysis of data and reviewing the manuscript. Ricardo Buitrago contributed in study design and collection of data. Rafael Beltrán contributed in study design and interpretation of data. Jairo Carreño contributed in analysis and interpretation of data and reviewing the manuscript. Carlos Carvajal contributed in study design, analysis and interpretation of data, writing and reviewing the report.

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## Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

## Ethical approval

The ethics committee at our institution approved the protocol before collecting patient's data from clinical records (N° CEI-00643-21) and supervised by an independent clinical monitoring group.

## Declaration of competing interest

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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