Placement of Inferior Vena Cava Filter: Clinical and Prognostic Characteristics of Cancer Patients at INCA

Filtro de Veia Cava Inferior: Características Clínicas e Prognósticas de Pacientes Oncológicos do INCA

Filtro de Vena Cava Inferior: Características Clínicas y Prognósticas de Pacientes con Câncer em INCA

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ABSTRACT

Introduction: Venous thromboembolism is a potentially fatal condition and frequent in oncologic patients. Quite often full anticoagulation is unfeasible, and placement of an inferior vena cava (IVC) filter becomes an option. Clinical indication, however, is controversial and expensive. **Objective:** To describe the demographic, clinical and epidemiological characteristics of oncologic patients submitted to IVC filter placement and their impact on global survival. **Method:** Retrospective cohort study with patients undergoing cancer treatment at INCA submitted to IVC filter placement from January 2015 to April 2017. Time between cancer diagnosis and death from any cause was considered for the analysis of the global 5-years survival. Descriptive analysis, survival estimates (Kaplan-Meyer) and Cox regression were performed. **Results**: 74 patients with a mean age of 54 (+15) years were included. Most of them had gynecological (52.7%) and digestive (20.3%) tumors. The median time between cancer diagnosis and IVC filter placement was 3.48 months (0-203). In the follow-up, 40 deaths (54.1%) were observed with a median time of 25 months (95% CI; 1.76 to 47.32). In the adjusted analysis, 5.63 times greater risk of death was verified in patients with IVC filter placement within six months after cancer diagnosis (HR=4.99; 95% CI; 2.20-11.33; p<0.001), and 2.47 times greater risk among those who did not do it at pre-operation (HR=2.47; 95% CI; 1.08-5.66; p=0.032). **Conclusion:** IVC filter placement was performed more frequently in patients with gynecological tumors and in until six months after cancer diagnosis was associated with increased risk of death.
Key words: Vena Cava Filters/adverse effects; Neoplasms; Venous Thromboembolism; Survival Analysis; Death.

RESUMO

Introdução: O tromboembolismo venoso é uma condição potencialmente fatal e frequente no paciente oncológico. Muitas vezes, a anticoagulação é inviável, e a colocação do filtro de veia cava (FVC) torna-se uma opção. A indicação clínica, entretanto, é controversa e gera alto custo. **Objetivo:** Descrever as características demográficas, clínicas e epidemiológicas dos pacientes com colocação de FVC e seu impacto na sobrevida global. **Método:** Estudo de coorte retrospectiva com pacientes em tratamento oncológico no INCA, que tiveram FVC implantado de janeiro/2015 até abril/2017. Na análise de sobrevida global em cinco anos, foram considerados o tempo entre o diagnóstico de câncer e o óbito por qualquer causa. Realizaram-se análise descritiva, estimativas de sobrevida (Kaplan-Meier) e regressão de Cox. **Resultados**: Foram incluídos 74 pacientes com média de idade 54 (+-15) anos. Em sua maioria, apresentavam tumores ginecológicos (52,7%) e digestivos (20,3%). O tempo mediano entre o diagnóstico de câncer e a colocação do FVC foi de 3,48 meses (0-203). No seguimento, foram observados 40 óbitos (54,1%) com mediana de tempo de 25 meses (IC 95%; 1,76-47,32). Na análise ajustada, verificou-se risco 5,63 vezes maior de morrer nos pacientes com colocação do FVC em até seis meses após o diagnóstico de câncer (HR=4,99; IC 95%; 2,20-11,33; p<0,001), e risco 2,47 vezes maior entre aqueles que não fizeram no pré-operatório (HR=2,47; IC 95%; 1,08-5,66; p=0,032). **Conclusão:** A colocação do FVC foi realizada com maior frequência em pacientes com tumores ginecológicos e em até seis meses após o diagnóstico de câncer foi associada a maior risco de óbito.
Palavra-chave: Filtros de Veia Cava/efeitos adversos; Neoplasias; Tromboembolia Venosa; Análise de Sobrevida; Morte.

RESUMEN

Introducción: El tromboembolismo venoso es una afección potencialmente mortal y frecuente en pacientes con cáncer. La anticoagulación a menudo no es factible, y la colocación de un filtro de vena cava (FVC) se convierte en una opción. Sin embargo, las indicaciones clínicas son controvertidas y generan un alto costo. **Objetivo:** Describir las características demográficas, clínicas y epidemiológicas de los pacientes con colocación de CVF y su impacto en la supervivencia general. **Método:** Estudio de cohorte retrospectivo de pacientes sometidos a tratamiento contra el cáncer en INCA a quienes se les implantó FVC entre enero de 2015 y abril de 2017. En el análisis de la supervivencia general a cinco años, el tiempo transcurrido entre el diagnóstico de cáncer y la muerte cualquier causa Se realizó un análisis descriptivo, estimaciones de supervivencia (Kaplan-Meier) y regresión de Cox. **Resultados**: Se incluyeron 74 pacientes con una edad media de 54 (+-15) años. La mayoría de ellos tenían tumores ginecológicos (52,7%) y digestivos (20,3%). La mediana del tiempo entre el diagnóstico de cáncer y la colocación de FVC fue de 3,48 meses (0-203). En el período de seguimiento, se observaron 40 muertes (54,1%) con una mediana de tiempo de 25 meses (IC 95%: 1,76 a 47,32). En el análisis ajustado, se observó un riesgo de muerte 5,63 veces mayor en pacientes con colocación de FVC dentro de los seis meses posteriores al diagnóstico de cáncer (HR=4,99; IC 95%: 2,20-11,33; p<0,001) y 2,47 veces mayor riesgo entre aquellos que no lo hicieron antes de la operación (HR=2,47; IC 95%; 1,08-5,66; p=0,032). **Conclusión**: La colocación de FVC se realizó con mayor frecuencia en pacientes con tumores ginecológicos. La colocación de FVC dentro de los seis meses posteriores al diagnóstico de cáncer se asoció con un mayor riesgo de muerte.
Palabras clave: Filtros de Vena Cava/efectos adversos; Neoplasias; Tromboembolia Venosa; Análisis de Supervivencia; Muerte.

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INTRODUCTION

Venous thromboembolism (VTE) is a potentially fatal condition with a close relation to cancer. Patients with neoplasms have more incidence of thromboembolic events in its clinical evolution[1,2]. Standard treatment is full anticoagulation, however, the oncologic patient can present clinical situations that impede its placement. Quite often it is necessary the mechanic interruption of the inferior vena cava (IVC) with the placement of a filter because of the difficulty of defining an effective drug treatment further to the risk of thrombosis recurrence and pulmonary embolism (PE)[3]. In the literature, clinical indications for inferior vena cava (IVC) filter placement are controversial and frequently based on experts opinions[4]. The most common indications are the presence of proximal venous thrombosis in patients with contraindication for full anticoagulation and the presence of isolate pulmonary thromboembolism and contraindication to anticoagulation[3].

The benefits of inferior vena cava filter in oncologic patients are still controversial in the literature. Two randomized trials did not reveal the benefits of IVC filter in the global survival, recurrence of VTE or mortality[5,6]. IVC filter is not recommended as well for patients in use of anticoagulant drugs[3].

Based in the knowledge of the demographic and clinical profile of patients submitted to IVC placement and the prognosis, it will be possible to guide individualized conducts in order to identify patients benefitting from this technique apart from those for whom clinical and prognostic benefit do not exist.

In this context, the objective of this study was to describe the demographic, clinical and epidemiological characteristics of oncologic patients submitted to IVC filter placement and analyze its impact in the global survival.

METHOD

Cohort prospective study carried out with patients in oncologic treatment in the National Cancer Institute José Alencar Gomes da Silva (INCA) for whom IVC filter was placed from January 2015 to April 2017. Patients whose physical chart was unable to be found were excluded. They were identified through active search according to procedure registered in the billing system. 76 patients were identified, two excluded because the physical chart was not found.

The data were extracted from electronic and physical charts. Demographic (age at the diagnosis of cancer, gender) and clinical information (topography of the tumor, type of thromboembolic event, time between cancer diagnosis and IVC filter placement, time between IVC filter placement and death) were obtained. For the evaluation of the indications of filter placement, international consensus criteria were followed in the analysis. Five-years global survival analysis considered the time between the diagnosis of cancer and the event (death for any cause). If death and loss to follow up are not registered, the cases were censored in the date of the last consultation entered in the chart or in the end of the 12 months follow up at the least.

Means and standard deviation (SD) for the continuous variables and distribution of frequencies for the categorical were utilized for the descriptive study of the population. For the univariate survival estimates, the Kaplan-Meier method was adopted, and Log-Rank test was used to calculate the statistical significance. Cox univariate regression was performed and for multiple regression, those with $p<0.20$ were selected. The final model was elaborated by the method Stepwise Forward, being retained the variables with $p<0.05$. All the analyzes were calculated with the statistical package SPSS (SPSS version 23.0, Inc. – Chicago, IL-USA, 2004).

The Institutional Review Board of INCA approved the study on September 25, 2017, number CAEE 72535517.0.0000.5274.

RESULTS

74 oncologic patients were submitted to IVC filter placement during the study period. The mean age at the diagnosis of cancer was 54 years (SD 14.8), with tumors in female genital organs (52.7%) and in digestive organs (20.3%) mostly. The predominant event was VTE isolated (87.8%) and IVC filter placed with median of time of 3.48 months (0-203) after cancer diagnosis. The majority of the patients had the thromboembolic event in the course of the oncologic treatment (Table 1).

24 patients (32.4%) in pre-operation with classic indication according to the guideline of the American Society of Hematology 2019[7] were identified for VTE management and IVC filter placement during an event of DVT (deep venous thrombosis). 15 patients (20.27%) submitted to the procedure were observed, despite guarded prognosis and five (6.75%) already in palliative care. Twelve (16.21%) patients were in anticoagulant treatment and had indication for IVC filter placement because of a suggestion of exploratory laparotomy. During the period analyzed (data not presented in the table) no withdraw of IVC filter occurred.

In the follow up period, 40 deaths occurred (54.1%) with median of time of 25 months (CI 95%; 1.76-4732) (Figure 1).

Table 1. Tumor, clinical and demographical characteristics of the patients with IVC filter from January 2015 to April 2017 (n=74)

Variable	N (%)
Age at diagnosis	
Mean and standard deviation	54.5 (14.8)
Gender	
Female	56 (75.7%)
Male	18 (24.3%)
Topography of the tumor (ICD)	
Digestive organs	15 (20.3%)
Female genital organs	39 (52.7%)
Other topographies*	20 (27.0%)
Preoperative	
No	50 (67.6%)
Yes	24 (32.4%)
Thromboembolism	
Pulmonary	5 (6.8%)
Venous	65 (87.8%)
Pulmonary and venous	4 (5.4%)
Time between the diagnosis of cancer and placement of IVC filter (months)	
Median (minimum – maximum)	3.48 months (0 – 203)
Time between placement of IVC filter and death (months) (n=40)	
Median (minimum – maximum)	2.38 months (0.7 – 19.5)
Death	
No	34 (45.9%)
Yes	40 (54.1%)

Captions: *Respiratory and Intrathoracic system (n=2); Melanoma (n=1); Mesothelial tissue (n=1); Breast (n=2); Male genital organs (n=1); Urinary tract (n=1); Eyes, encephalon and others of the central nervous system (n=5); Hematological or lymphatic tissue (n=3); Malignant without other specifications (n=4). ICD: International Classification of Diseases; IVC: Inferior vena cava filter.

Figure 1. Time between the diagnosis of cancer and death (Kaplan-Meier method global survival curve) (n=74)
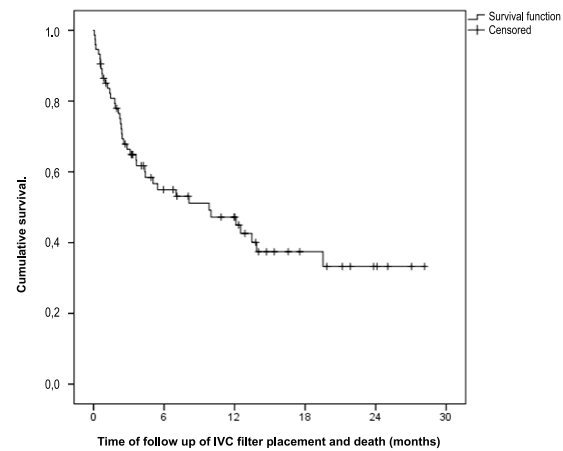
Figure 2. Time between IVC filter placement and death (Kaplan-Meier method global survival curve) (n=74)

The median time between the IVC filter placement and death was 9.8 months (CI 95%; 2.4-17.3) (Figure 2). Four deaths (5.4%) occurred in the first 30 days after IVC filter placement. Of the patients who died, 14 (35.0%) did not have formal indication for the procedure.

The patients with IVC filter placement in until six months after the diagnosis of cancer had mean survival time lower than the others (p<0.001). The other variables analyzed did not present statistically significant difference in global survival time (Table 2).

The adjusted analysis concluded there was 5.63 fold bigger odds of dying in patients who underwent IVC filter placement in six mon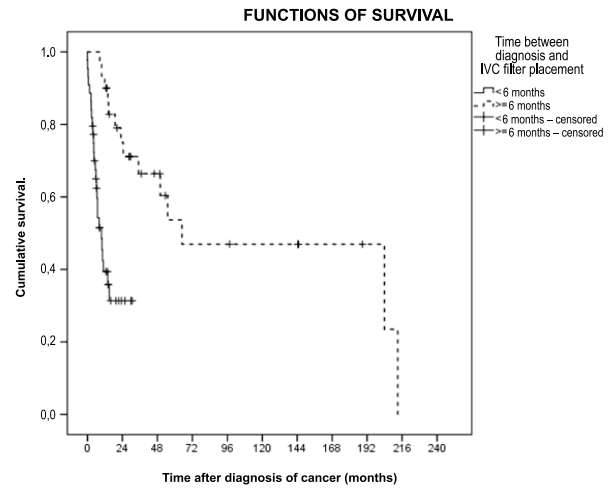ths after the diagnosis of cancer (HR=4.99; CI 95%; 2.20-11.33; p<0.001) and 2.47 fold bigger odds among those who did not undergo in pre-operation (HR=2.47; CI 95%; 1.08-5.66; p=0.032) (data not presented).

DISCUSSION

IVC filter placement was more frequent in patients with gynecologic tumors and in until six months after the diagnosis of cancer was associated to higher risk of death.

The management of anticoagulation in oncologic patients is still quite challenging. The patients oscillate between hemorrhagic and thrombotic risk and quite often, thrombosis occurs concomitantly with hemorrhage. In this scenario, IVC filter placement becomes a therapeutic option in cases of DVT with high risk of PE[8]. In our population, although removable IVC filters have been

Table 2. Time of global survival according to the clinical and demographic characteristics (n=78)

Variable	Death N (%)		Global survival	
	No	Yes	Mean (CI 95%)	P value
Age at diagnosis				
< 60 years	18 (52.9%)	25 (62.5%)	87.9 (55.0 – 120.9)	0.828
≥ 60 years	16 (47.1%)	15 (37.5%)	48.3 (22.9 – 73.6)	
Gender				
Female	24 (70.6%)	32 (80.0%)	73.9 (41.9 – 105.9)	0.529
Male	10 (29.4%)	08 (20.0%)	70.1 (33.9 – 106.3)	
Topography of the tumor (ICD)				
Digestive organs	08 (23.5%)	07 (17.5%)	39.3 (22.9 – 55.7)	
Female genital organs	17 (50.0%)	22 (55.0%)	82.2 (44.9 – 119.5)	0.667
Other topographies	09 (26.5%)	11 (27.5%)	52.2 (16.4 – 88.0)	
Preoperative				
No	17 (50.0%)	33 (82.5%)	66.0 (36.8 – 95.3)	0.087
Yes	17 (50.0%)	07 (17.5%)	120.1 (78.3 – 161.9)	
Indication of IVC filter				
No	13 (38.2%)	14 (35.0%)	93.6 (49.4 – 137.8)	0.379
Yes	21 (61.8%)	26 (65.0%)	68.2 (31.2 – 105.1)	
Time between diagnosis of cancer and placement of IVC filter (months)				
>= 6 months	16 (47.1%)	14 (35.0%)	115.2 (75.0 – 155.3)	<0.001
< 6 months	18 (52.9%)	26 (65.0%)	13.9 (10.1 – 17.8)	

Captions: ICD: International Classification of Diseases; IVC: Inferior vena cava filter; CI: Confidence Interval.

placed, no IVC filter was removed from any of the patients during the investigation.

Preventive measures and anticoagulation management is a great challenge for thromboembolic events in oncologic patients. The occurrence of DVT in patients with tumor hemorrhages and in other situations due to the own risk of fatal hemorrhage depending on the tumor site is frequent. In this context, the use of routines for indication of anticoagulant treatment or utilization of mechanic methods is aimed to facilitate its recommendation and allotment of financial resources for the benefit of the patients and of the institution for its good use, considering the cost-benefit for the patient and its quality of life.

Wassef et al.[3] presented similar results of the current study. In the study of Patel and Patel[9], the conclusion was that the placement of IVC filter caused no impact in the mortality. In oncologic patients with advanced disease, it should be considered priority for palliative clinical support that minimizes the patients' suffering. It must be verified the actual benefit of implementation of invasive conducts and of high institutional cost without advantages for the patient or impact in its quality of life.

The limitations of retrospective observational studies must be weighed regarding the quality of the information obtained in the charts. It was not possible to identify the actual *causa mortis* in the study population due to incomplete data in the death certificates which described the tumor site and progression of the disease as *causa mortis* mostly. However, it is attempted to review the follow up of the patients post IVC filter placement and its clinical conditions in the moment this procedure is indicated in order to improve the information collected.

CONCLUSION

The IVC filter placement was more frequent in patients with gynecologic tumors. DVT alone was the predominant event and most of the patients suffered the thromboembolic event in the course of the oncologic treatment. The IVC was placed with median time of 3.48 months after cancer diagnosis. In the follow up period, 40 deaths (54.1%) occurred and IVC filter placement in until six months after the diagnosis of cancer was associated to higher risk of death.

CONTRIBUTIONS

Marcos Renni contributed for the study conception and/or design, collection, analysis and interpretation of

the data, wording, and critical review with intellectual contribution. Anke Bergmann contributed for the study conception and/or design, collection, analysis, and interpretation of the data. Andreia Cristina de Melo contributed for the wording and critical review with intellectual contribution. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

The author Anke Bergmann declares potential conflict of interests for being scientific editor of the Brazilian Journal of Cancerology of INCA. The other authors have no conflict of interests.

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