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# Inferior Vena Cava Filter as Management of Venous Thromboembolism Associated With Malignancy: A Systematic Review

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## Abstract

**Introduction**. The risk of venous thromboembolism (VTE) associated with malignancy is 4.1-fold greater compared to patients without malignancy. Malignancy patient have greater risk of bleeding with the commonly used anticoagulant therapy. Inferior Vena Cava Filter (IVCF) have been recommended as an controversial alternative. This study aimed to find the highest evidence in the safety, benefit, and clinical outcome of the IVCF for managing VTE associated with malignancy.

**Method**. Aligning with PRISMA guidelines, online databases Cochrane, PubMed, ScienceDirect and ClinicalKey were searched using keywords ("*Inferior Vena Cava Filter*" or "IVCF") and (“*Anticoagulant*”) and ("*Cancer*" or "*Malignancy*") and ("*Venous Thromboembolism*" or "VTE" or "*Pulmonary Embolism*" or "*Deep Vein Thrombosis*") and ("*Safety" or "Benefit" or "Complication" or "Recurrence" or "Survival Rate" or "Mortality*"). These articles were reviewed and appraised to find out the level of evidence.

**Results**. There were 10 articles reviewed (1,191 participants). Complication of IVCF found: filter migration (0.9%), vena cava thrombosis (3.7%), recurrent PE (2.8%); filter fracture (0.9%); and IVCF penetration (0.9%). No mortality was found in patients due to complications due to filter insertion (LOE 2). IVCF insertion can reduce PE rates but with an increase in the number of DVT (DVT: with filter vs without filters: 35.7% vs 27.5%; HR 1.52; CI95 % 1.02–2.27; p = 0.042 ; PE: 6.2% vs. 15.1%; HR 0.37; 95% CI 0.17–0.79; p = 0.008). Six studies found no statistically significant increase in PE-related mortality.

**Conclusion**. IVCF is safe and beneficial for the management of malignancy associated VTE, especially in patients with contraindications to anticoagulants (LOE 2, 3 and 4).

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**Keywords**: *inferior vena cava filter, venous thromboembolism, malignancy, safety, benefit, complication, recurrence, mortality*

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## Introduction

Approximately 20% of all cases of venous thromboembolism (VTE) experienced by patients with malignancy. VTE is divided into two major groups, deep vein thrombosis (DVT) and pulmonary embolism (PE). According to Shen and Pollak, the cause of death of one in seven cancer patients hospitalized is due to PE.[1] The underlying mechanism is multifactorial, one of them is hypercoagulability. Other contributing factors are venous compression due to tumor growth, thrombocytosis, immobility, chemotherapy or radiation therapy.[2] Bouillaud and Trousseau reported an association between thromboembolism and hypercoagulability in cases of malignancy.[3,4] The risk of venous thromboembolism (VTE) associated with malignancy is 4.1-fold greater compared to patients without malignancy.[5,6]

Malignancy patients have greater risk of bleeding with the commonly used anticoagulant therapy. The American College of Chest Physician Society (ACCPS) in 2012 already recommends the use of an inferior vena cava filter (IVCF) for patients with contraindications to anticoagulants.[7] However, the use of IVCF is not free from controversy because several studies still question its safety and benefits over pharmacological anticoagulants.[9] This study aimed to find the highest evidence in the safety, benefit, and clinical outcome of the IVCF for managing VTE associated with malignancy.

## Method

A study of systematic review conducted in accordance with preferred reporting items for systematic review and meta-analysis protocols (PRISMA). Literature search proceeded on Cochrane, PubMed, Science Direct and ClinicalKey using keywords ("*Inferior Vena Cava Filter*" or "IVCF") and ("*Anticoagulant*") and ("*Cancer*" or "*Malignancy*") and ("*Venous Thromboembolism*" or "VTE" or "*Pulmonary Embolism*" or "*Deep Vein Thrombosis*") and ("*Safety" or "Benefit" or "Complication" or "Recurrence" or "Survival Rate" or "Mortality*") as in **Table 1**.

All articles focused on IVCF as management of VTE in malignancy patients published in English, available in full text and without year limitation. These articles were reviewed and appraised for the

study design used, enrolled samples, validation of results.

**Results**

On literature search, a total of 71 articles found from PubMed and 14 articles found from ScienceDirect. After screening up, a total of 10 articles enrolled, including six case series, one case control, one randomized controlled trial, and two cohort. Critical analysis and data extraction were carried out, focused on the follow-up duration, survival rate, mortality associated with PE, VTE recurrence and complication. These articles were listed on **Table 2** and **Table 3** including the level of evidence.

**Discussion**

All authors stated that there were no complications of IVCF at the time of insertion. Losseff and Decouscus did not find any complications due to the use of IVCF significantly in VTE patients related to clinically proven malignancy.[10,11] Schunn, Wallace, Myojo, Mansour, and Craven experienced complications due to the use of IVCF in the form of PE, new thrombosis, maldeployed filter , but not statistically significant,[9,12–15] whereas Damascelli found 16 complications in seven patients: one migration (0.9%), four cases of vena cava thrombosis (3.7%), three of which were associated with recurrent PE (2.8%); one filter fracture (0.9%); and one IVCF penetration (0.9%). Changes in filter slope greater than 15° occurred in six patients (5.7%).[16] Mansour found that patients with IVCF had more frequent complications of DVT than those without filters (35.7% vs 27.5%; HR 1.52; CI95 % 1.02–2.27; p = 0.042 but significantly fewer PE symptoms (6.2% vs. 15.1%; HR 0.37; 95% CI 0.17–0.79; p = 0.008) and concluded that the use of IVCF can reduce PE rates but with an increase in the number of DVT.[14] Abtahian reported IVC thrombosis in 2–30% of patients, and DVT in 20% of patients.[17] Narayan reported no statistically significant difference in the use of IVCF.[18]

Losseff, Schunn, Wallace, Myojo, Abtahian and Mansour found no significant recurrence of PE in their study.[9,11–14,17] Decouscus found that the recurrence rate of PE with IVCF was 1.1% and without IVCF was 4.8. %.[10] Damascelli found recurrence of PE in three of 58 patients (5.2%).[16] Abtahian reported a PE recurrence rate of 1% to 7%.[50] Craven reported that 10 of 44 patients had recurrent PE.[17] In his study, Craven found that patients on IVCF had a lower overall survival than patients with malignancy who received anticoagulation.[15] This could be explained, because the majority of patients treated

with IVCF had disease at an advanced stage while the majority of patients treated with anticoagulants were at an early stage.

Damascelli, Schunn, Myojo, Mansour, Losseff, and Craven found no statistically significant increase in PE-related mortality.[11–16] Decouscous found death in one in six IVCF patients from PE compared to five in 12 without IVCF (p = 0.16), no significant difference in mortality from IVCF.[10] Wallace documented 1.3% PE-related deaths.[9] Narayan found that patients did not gain any additional survival benefit from IVCF placement.[18]

The limitation of this study, safety and benefits of IVCF is difficult to obtain without a randomized method and an appropriate control group to compare cancer patients with IVCF and without IVCF. Only two studies, namely Schunn and Decousus, reported clinical outcomes from a control group according to age, sex, type of malignancy, and stage of disease.[10,12] Meanwhile, other studies compared the use of IVCF in VTE patients with malignant and non-malignant.

Only five studies conducted studies in multicenters (Narayan, Damascelli, Schunn, Wallace, and Decousus) and four studies reported small sample sizes (Schunn, Abathian, Mansour and Myojo). Other constraints found were in terms of the appropriate evaluation method to identify the clinical impact caused by IVCF and the limitation of the follow-up period after IVCF placement. All of these limitations make it difficult to account for possible bias.

Wallace and Myojo had difficulty controlling for confounding factors to identify complications caused by IVCF, and did not stratify patients according to the stage of malignancy, nor did they significantly examine survival between malignant and non-malignant patients.[9,13] Schunn and Abtahian have limitations in the form of selection bias. due to miscoding and the low probability of thromboembolic complications due to the lack of prospective screening, as well as the use of a small sample size, resulting in a type 2 error.[12,17] Mansour and Myojo have a small sample size.[13,14] Narayan has a high loss to follow-up rate and limitations. long-term complications that arise, because the study was limited to 30 days post-IVCF insertion.[18]

This indicates that although the available data show the use of IVCF with malignancies at high risk of VTE is quite

effective, it still has some methodological limitations. There is even one study that does not explain its limitations, namely the study by Decousus et al.[10] For the effects of anticoagulants compared directly with IVCF, studies are limited in terms of increased morbidity and mortality in patients with VTE-associated malignancy.

## Conclusion

From this systematic review, we can concluded that IVCF is beneficial and safe for use in cases of malignancy-associated VTE in terms of complications due to filter insertion, PE recurrence and increased PE-related mortality compared to anticoagulants (LOE 2, 3 and 4). No mortality was found in patients due to complications due to filter insertion (LOE 2). The use of IVCF can reduce the recurrence of PE (LOE 4). The cause of death in the population studied was due to underlying malignancy, not recurrence of PE or use of IVCF (LOE 4). Common indications for the use of IVCF are contraindications to anticoagulants and as VTE prophylaxis. The use of IVCF has been shown to be effective and safe in clinically preventing PE, although there are limited advantages in survival rates in patients with end-stage malignancy and the presence of metastases.

Evaluation method using serial ultrasound to definitively assess IVCF position can reduce complications due to IVCF use and reduce further treatment costs. It is necessary to conduct future studies on IVCF alternative management in patients with malignancy. More multicenter RCT studies comparing malignant patients with IVCF are needed to better convince clinicians of the safety and benefits of PE prophylaxis, complications, survival, and costs over pharmacological prophylaxis.

## Disclosure

Authors disclose there was no conflict of interest.

## Acknowledgement

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**List of Tables**

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**Table 1. Terminology used in databases**

| Database | Terminology | Hit |
|---|---|---|
| Cochrane | "Inferior Vena Cava Filter" OR "IVCF" in Title, Abstract, Keywords AND "Anticoagulant" in Title, Abstract, Keywords AND "Cancer" OR "Malignancy" in Title, Abstract, Keywords AND "Venous Thromboembolism" OR "VTE" OR "Pulmonary Embolism" OR "Deep Vein Thrombosis" in Title, Abstract, Keywords AND "Safety" OR "Benefit" OR "Complication" OR "Recurrence" OR "Survival Rate" OR "Mortality" in Title, Abstract, Keywords | 0 |
| ClinicalKey | "Inferior Vena Cava Filter" OR "IVCF" in Title, Abstract, Keywords AND "Anticoagulant" in Title, Abstract, Keywords AND "Cancer" OR "Malignancy" in Title, Abstract, Keywords AND "Venous Thromboembolism" OR "VTE" OR "Pulmonary Embolism" OR "Deep Vein Thrombosis" in Title, Abstract, Keywords AND "Safety" OR "Benefit" OR "Complication" OR "Recurrence" OR "Survival Rate" OR "Mortality" in Title, Abstract, Keywords | 0 |
| Pubmed | (((((Inferior Vena Cava Filter[Title/Abstract]) OR (IVCF[Title/Abstract])) AND (Anticoagulant[Title/Abstract])) AND ((Cancer[Title/Abstract]) OR (Malignancy[Title/Abstract]))) AND ((((Venous Thromboembolism[Title/Abstract]) OR (VTE[Title/Abstract])) OR (Pulmonary Embolism[Title/Abstract])) OR (Deep Vein Thrombosis[Title/Abstract]))) AND ((((((Safety[Title/Abstract]) OR (Benefit[Title/Abstract])) OR (Complication[Title/Abstract])) OR (Recurrence[Title/Abstract])) OR (Survival Rate[Title/Abstract])) OR (Mortality[Title/Abstract])) | 71 |
| Science Direct | "Inferior Vena Cava Filter" OR "IVCF" in Title, Abstract, Keywords AND "Anticoagulant" in Title, Abstract, Keywords AND "Cancer" OR "Malignancy" in Title, Abstract, Keywords AND "Venous Thromboembolism" OR "VTE" OR "Pulmonary Embolism" OR "Deep Vein Thrombosis" in Title, Abstract, Keywords AND "Safety" OR "Benefit" OR "Complication" OR "Recurrence" OR "Survival Rate" OR "Mortality" in Title, Abstract, Keywords | 14 |

**Table 2.** Study characteristics

| No. | Study, Year | Country | Study Design | Subject | Age median/ mean (year) | Follow-up duration (days) | LOE |
|---|---|---|---|---|---|---|---|
| **1** | Lossef et al, 1995 [11] | USA | retrospective studies, case series | **34**<br>stage III malignancy: 17 (50%)<br>stage IV malignancy: 16 (47%)<br>CML : 1 (3%)<br><br>35 IVCF placed<br>DVT : 21 (60%)<br>PE : 10 (28,6%)<br>PE and DVT : 4 (11,4%) | 61 (25-87) | 840<br>(Mean 5,2) | **4** |
| **2** | Decousus et al, 1998 [10] | USA | Randomizied clinical trial | **400**<br>Filter group : 200 (50%)<br>Non Filter group : 200 (50%)<br><br>among them there are **56 patients with malignancy**<br>Filter group : 32 (16%)<br>Non Filter group : 24 (12%) | Filter group : 73±11<br>Non filter group : 72±11,5 | 12 and 730 | 2 |
| **3** | Wallace et al, 2004 [9] | USA | retrospective studies, case series | **308**<br>Solid tumor : 267 (86,7%)<br>Liquid tumor : 41 (13,3%) | 60 (24 – 81) | 30, 90, and 365 | 4 |
| **4** | Schunn et al, 2006 [12] | USA | retrospective studies, descriptive, case control | **134**<br><br>Among them there are **55 patients with stage III and IVmalignancy**<br>DVT : 42 (76,4%)<br>PE : 6 (10,9%)<br>PE and DVT : 7 (12,7%) | Median 58<br>Mean 60,9 ±1,87 | 248,3 ± 48,5 | **3** |
| **5** | Damascelli et al, 2011[16] | Italy | prospective observational (cohort) | **106**<br>DVT : 48 (45,3%)<br>PE : 5 (4,7%)<br>PE and DVT : 53 (50%) | 61,5 (18–87) | 319,4<br>(118 –1,388) | **3** |

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| No. | Study, Year | Country | Study Design | Subject | Age median/ mean (year) | Follow-up duration (days) | LOE |
|---|---|---|---|---|---|---|---|
| **6** | Mansour et al, 2014 [14] | Jordan | retrospective studies, descriptive, case series | **107**<br>DVT : 76 (71,0%)<br>PE : 14 (13,1%)<br>PE and DVT : 17 (15,9%)<br>Among them there are **81 patients with stage III and IVmalignancy** | 50,8 ±14,2 | 90 | **4** |
| **7** | M Myojo et al, 2015 [13] | Japan | clinical investigation, case series | **26**<br>with rIVCF : 25<br>with IVCF : 1<br>(IVCF retrieval : 7) | 66,6 ± 13,8 | 467,8 (20–1857) | 4 |
| **8** | Abtahian et al, 2014 [17] | USA | retrospective studies, clinical research, case series | **666** (with rIVCF)<br>among them there are **247patients with malignancy** (37,1%) | 64,3 ± 11,6 | 401,0 | 4 |
| **9** | A Narayan et al, 2016 [18] | USA | retrospective cohort | **672**<br>among them there are **246 patients with malignancy** (36,6%)<br>Carcinoma type: 151 (22,7%)<br>Sarcoma type: 92 (13,8%)<br>Mixed type: 4 (0,6%) | Patients with malignancy: 61,9 ± 13,6<br>without malignancy: 57,4 ± 16,8 | 30 | 2 |
| **10** | Craven et al, 2018 [15] | Australia | retrospective studies, observational, case series | **45**<br>DVT : 14 (31,1%)<br>PE : 15 (33,3%)<br>PE and DVT : 13 (28,9%)<br>Without PE or DVT : 3 (6,7%)<br>among them there are **32 patients with malignancy** (71,1%) | Mean 64.4 ±15,3<br>Median 66 (21 – 92) | 730 | **4** |

**Note :**
CML = Chronic Myelogenous Leukemia, DVT = Deep Vein Thrombosis, IVCF = Inferior Vena Cava Filter, PE = Pulmonary Embolism, rIVCF = retrievable Inferior Vena Cava Filter, USA = United States of America

**Table 3.** Clinical outcome of IVCF placement in malignancy associated VTE patients

| No. | Study | Mortality associated to PE | PE recurrence | Complication | Study limitation |
|---|---|---|---|---|---|
| **1** | Lossef et al, 1995 [11] | Survival rate after 1 day – 28 months :<br>- Mean survival time<br>Stage III : 8,0 months<br>Stage IV : 5.5 months<br>- Alive > 3 months<br>Stage III : 93%<br>Stage IV : 4.59%<br>Survival rate combined for all patients is 6.6 months<br>- Discharge alive : 82%<br>- Discharge to homecare : 61%<br>- Death before hospital discharge : 6 (18%)<br>(1 death suspect due to PE) | None | None | Single center |
| **2** | Decousus et al, 1998 [10] | - In 12 days duration<br>Filter group : 1.1%<br>Non filter group : 4.8%<br>(p = 0.03)<br>- In 2 years duration<br>Filter group : 6 patients had PE with 1 death<br>Non filter group : 12 patients had PE with 5 death | - Filter group : 37 (20.8%)<br>- Non filter group : 29 (15.5%) | 12 days duration<br>- On filter group<br>5 death caused by :<br>bleeding, myocard infarct, acute kidney failure<br>- On non filter group<br>5 death caused by:<br>4 PE and 1 infection | Not mentioned |
| **3** | Wallace et al, 2004 [9] | Median Survival rate on day-30, 90, and 365:<br>- Patients with solid tumor :<br>0.81, 0.60, and 0.35<br>- Patients with liquid tumor :<br>0.85, 0.67, 0.48 | 4 from 308 patients (1.2%) | From 308 patients<br>- Recent thrombosis: 14 (4.5%)<br>- Retroperitoneal bleeding: 2 (0.6%)<br>- Maldeployment filter: 2 (0.6%) | - Retrospective study and difficult to control confounders to identify complications caused by filters<br>- Researchers did not stratify patients based on the stage of malignancy and did not |

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| No. | Study | Mortality associated to PE | PE recurrence | Complication | Study limitation |
|---|---|---|---|---|---|
| | | | | | perform a significant survival analysis between malignant and non-malignant patients. |
| **4** | Schunn et al, 2006 [12] | - Mean survival rate : 259.2 (±45 SE) days<br>- Median survival rate : 145 days<br>- There are 23.6% death in 30days after IVCF placement<br>- Alive < 3 months : 41.8%<br>- Alive > 6 months : 54.5% | 3 patients (5.5%) | - Filter thrombosis : 1 (1.8%) | - Selection bias due to miscoding and fewer thromboembolic complications due to lack of prospective screening<br>- Small number of samples, resulting in type 2 error |
| **5** | Damascelli et al, 2011[16] | - Zero mortality due to PE (0%)<br>- 2 from 58 patients dies of underlying disease | 3 from 58 patients (5.2%) | DVT recurrence not found<br>There are 16 complications in 7 patients:<br>- Filter migration: 1 (0.9%),<br>- Vena Cava thrombosis : 4 (3.7%),<br>- Filter fracture : 1 (0.9%),<br>- Changes in filter slope >15° : 6 (5.7%) | - No control group : All patients were placed on IVCF and given a low dose of anticoagulant |
| **6** | Mansour et al, 2014 [14] | - Median survival rate for all groups: 2.39 months (range: 0.03–60.2)<br>- Median survival rate for stage III and IV malignancy patients: 7.97 months (1.90–17.08) and 1.31 months (0.92–2.20) (p = 0.0119) | 3 patients (2.8%) | - DVT recurrence: 10 patients (9.35%)<br>- Filter Thrombosis : 1 patients (0.01%) | - Small samples<br>- Conducted in single center |

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| No. | Study | Mortality associated to PE | PE recurrence | Complication | Study limitation |
|---|---|---|---|---|---|
| **7** | M Myojo et al, 2015 [13] | - 1 year Survival rate: 46%<br>- 2 year Survival rate: 18% | No observations made | Filter penetration happened on 3 patients<br>- Gunther Tulip filter: 2<br>- ALN filter: 1 (perforation to the aorta but no symptoms found during observation) | - Confounding factors are difficult to exclude<br>- Small samples<br>- Conducted in single center only |
| **8** | Abtahian et al, 2014 [17] | - Survival rate of 115 malignant patients with metastases<br>30 days: 94 (81.7%)<br>90 days: 81(70.4%)<br>180 days: 63(54.8%)<br>365 days: 43 (37.4%)<br>- Survival rate 132 malignant patients with no metastases<br>30 days: 125 (94.7%)<br>90 days: 111 (84.1%)<br>180 days: 103 (78.0%)<br>365 days: 85 (64.4%) | - Of 115 malignant patients with metastases:<br>12 (10.4%)<br>- Of 132 malignant patients with no metastases:<br>3 (2.3%) | Of 115 malignant patients with metastasis<br>IVC thrombosis: 5 (4.3%)<br>DVT : 15 (13.0%)<br>- Of 132 malignant patients with no metastasis:<br>IVC thrombosis: 1 (0.8%)<br>DVT : 18 (13.6%) | - Selection bias<br>- No control group (where patients were not placed IVCF)<br>- Conducted in single center only |
| **9** | A Narayan et al, 2016 [18] | - Malignant patients with metastases had a lower probability of survival at 30 days, 1 year, and 5 years (73%, 27%, 10%) compared to patients without metastases at baseline (82%, 43%, 20%) | 30day follow-up:<br>- Patients with malignancy: 4.1 %<br>- Patiensts with no malignancy: 1.8 %<br>Statistically, this result was significant using multivariate analysis (RR 2.7 [95% CI 1.0, 7.5]) but not significant using the Cox model (HR 2.2 [95% CI, 0.8, 5.7 ]) | 30day follow-up :<br>- VTE<br>Patients with malignancy: 13.4%<br>Patiensts with no malignancy: 7.7%<br>Statistically, these results were significant using multivariate analysis (RR 2.0 [95% CI 1,2, 3,3]) and the Cox model (RR 1.9 [95% CI 1.1, 3.2]).<br>- DVT or IVC thrombosis | - High loss to follow up rate<br>- Long-term complications that arise, because the study was limited to 30 days after IVCF placement |

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| No. | Study | Mortality associated to PE | PE recurrence | Complication | Study limitation |
|---|---|---|---|---|---|
| | | | | Patients with malignancy: 10.6%<br>Patiensts with no malignancy: 8%<br>Statistically, these results were significant using the multivariate analysis (RR 1.7 [95% CI, 1.0, 3.1]) and the Cox model (HR 1.7 [95% CI, 1.0, 3.0]). | |
| **10** | Craven et al, 2018 [15] | 17 patients death caused by underlying disease | 1 case | - IVCF tilting : 2<br>- Filter thrombosis: 3<br>- Recurrence DVT : 2 | - Conducted in single center only |

**Note :**
CI = Confidence Interval, DVT = Deep Vein Thrombosis, HR = Hazard Ratio, IVC = Inferior Vena Cava, IVCF = Inferior Vena Cava Filter, PE = Pulmonary Embolism, RR = Relative Risk, SE = Standard Error

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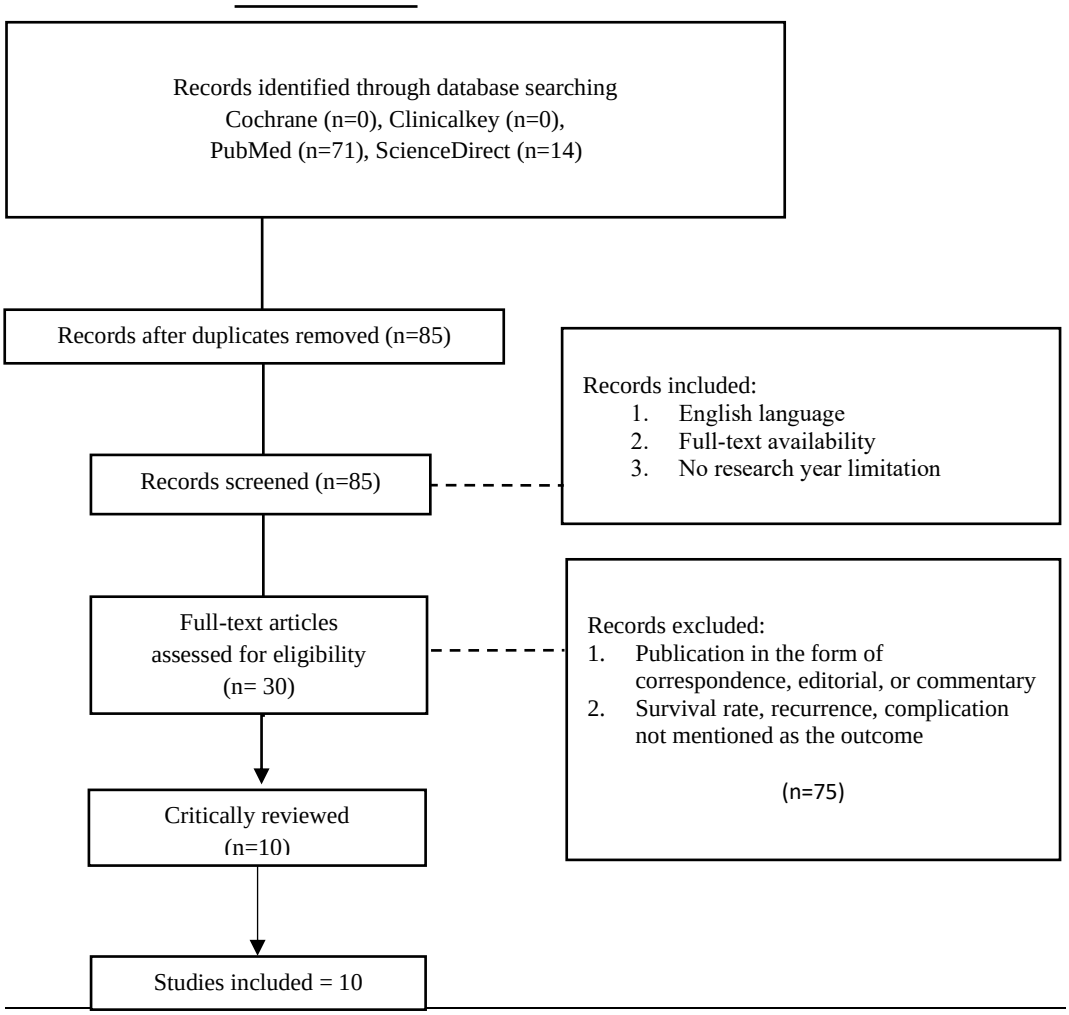


**Figure 1**. Flowchart of search strategy