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CLINICAL REVIEW

Comparative Meta-analysis of Catheter-Directed Thrombolysis Plus Anticoagulation vs Anticoagulation Alone in Acute Lower-Limb Deep Venous Thrombosis Treatment

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Abstract

Objective: Catheter-directed thrombolysis (CDT) has emerged as a potential therapeutic option for deep vein thrombosis (DVT), offering the ability to improve post-thrombotic syndrome (PTS) and enhance iliofemoral vein patency. Nevertheless, concerns have been raised regarding complications such as pulmonary embolism (PE), bleeding incidents, and extended hospital stays. This study systematically reviewed relevant research articles and conducted a comprehensive meta-analysis to compare the outcomes of CDT in combination with anticoagulation therapy vs anticoagulation therapy alone. **Methods:** We independently extracted data from a total of 17 articles and performed statistical analyses using SPSS Statistics (version 29.0) and Review Manager (version 5.1). **Results:** Our analysis revealed that CDT demonstrated potential for improving PTS (95% confidence interval [CI] 0.29, 0.51; $P<.00001$; $I^2 = 55\%$) and increasing iliofemoral vein patency (95% CI 1.78, 3.02; $P<.00001$; $I^2 = 70\%$) when compared with anticoagulation therapy alone. However, the CDT group exhibited a higher incidence of PE ($P<.00001$, $I^2 = 47\%$) and prolonged hospital stays ($P = .01$, $I^2 = 87\%$) compared with the group receiving anticoagulation therapy alone. Moreover, we observed an increased risk of bleeding events associated with CDT treatment ($P<.00001$, $I^2 = 40\%$). However, there was no significant difference in recurrent venous thromboembolism ($P = .05$, $I^2 = 0\%$) or mortality ($P = .20$, $I^2 = 43\%$) between the 2 groups. **Conclusion:** This meta-analysis suggests that CDT can improve the patency of iliofemoral veins when compared with anticoagulation alone, leading to a reduction in PTS. However, it should be noted that the CDT group experienced a higher incidence of bleeding and PE events, as well as a longer average duration of hospital stay compared with the anticoagulation group. On the other hand, recurrent venous thromboembolism and mortality rates did not significantly differ between the 2 groups. Therefore, the benefits and risks of CDT should be carefully weighed on a case-by-case basis with consideration of the patient's individual risk factors and preferences.

Introduction

Deep vein thrombosis (DVT) occurring in the lower extremities is a highly prevalent medical condition, manifesting in a yearly incidence rate of 5 cases per 10,000 individuals within the population.[1] Notably, the frequency of DVT has exhibited a consistent upward trend among individuals aged 60 and above.[1] Manifestations of DVT vary in severity between proximal and distal vein thrombosis, and encompass leg pain, swelling, alterations in skin color, and sensation of localized warmth.

Profound complications may accompany DVT, encompassing the emergence of acute pulmonary embolism (PE) or venous limb gangrene due to phlegmasia cerulea or alba dolens. The development of post-thrombotic syndrome (PTS) is due to chronic venous insufficiency that ensues subsequent to an episode of proximal DVT, wherein clinical manifestations are known to vary among patients, ranging from mild edema to severe ulcerations, thereby significantly impairing their overall quality of life.

Traditional management of DVT primarily aims to prevent the occurrence of complications such as PE and PTS, alongside curtailing the risk of recurrence. Regrettably, it has been observed that over 50% of patients undergoing conventional treatment ultimately develop PTS following therapy.[2] In response to this clinical challenge, catheter-directed thrombolysis (CDT) has emerged as a therapeutic modality for DVT, offering superior efficacy in the dissolution of thrombotic deposits compared with anticoagulation therapy alone. By expediting clot removal, CDT yields more expeditious outcomes. Furthermore, CDT provides enhanced accessibility to the occlusion site, thereby diminishing the incidence of hemorrhagic complications.[3] CDT therapy is performed with the insertion of a catheter into the thrombosed vein through either the contralateral femoral vein, the right internal jugular vein, or the ipsilateral popliteal vein, enabling direct infusion of thrombolytic agents into the intraluminal thrombus, ensuring optimal delivery and maximizing their effectiveness.

In light of these developments, the objective of our meta-analysis is to comprehensively evaluate and contrast the clinical outcomes associated with CDT and conventional anticoagulation therapy. By synthesizing evidence from 17 comparable studies, we aim to delineate the relative effectiveness of these therapeutic approaches in patients affected by DVT.

Table 1. Baseline characteristics and demographic data of Included research studies.

Study	Study Type	Follow-up	Group	Sample	Mean age, years	Women, %
Young 2019[1]	Retro	5 years	CDT + AC	29	57.8	58.6
			AC	120	58	51.7
AbuRahma 2000[4]	Pro	60 months	CDT + AC	18	46	61.0
			AC	33	49	58.0
Elsharawy 2001[5]	RCT	6 months	CDT + AC	18	44	67.0
			AC	17	49	71.0
Riyaz 2014[6]	Retro	72 months	CDT + AC	3594	53.2	49.3
			AC	3594	65.4	49.2
Enden 2012[7]	RCT	2 years	CDT + AC	90	53.3	35.6
			AC	99	50	38.4
Lee[8]	Retro	15.2 months	CDT + AC	27	62.4	51.8
			AC	26	59.8	46.2
Enden 2009[9]	RCT	6 months	CDT + AC	50	53	64.0
			AC	53	51	60.4
Srinivas 2014[10]	Pro	6 months	CDT + AC	27	39	48.1

			AC	28	53	42.9
Haig 2016[11]	RCT	5 years	CDT + AC	87	58	39.0
			AC	89	53	75.0
Zhang 2013[12]	Retro	38 months	CDT + AC	47	NA	NA
			AC	81	NA	NA
Haig 2014[13]	RCT	24 months	CDT + AC	90	53.3	36.0
			AC	99	50	38.0
Notten 2020[14]	RCT	12 months	CDT + AC	77	49	63.6
			AC	75	52	69.3
Brailovsky 2020[15]	RCT	9 years	CDT + AC	1287	63.1	53.6
			AC	1287	62.2	53.9
Kim 2016[16]	Retro	30 months	PMI (CDT)	56	59.5	51.8
			ACA	46	52	43.5
Alkhouli 2014[17]	Retro	6 years	CDT + AC	563	52.1	44.3
			AC	563	51.4	48.5
Brailovsky 2014[18]			CDT + AC	309	NA	NA
			AC	306	NA	NA
Magnuson 2019[19]	RCT	24 months	CDT + AC	337	NA	NA
			AC	335	NA	NA

CDT = catheter-directed thrombolysis; AC = anticoagulation; NA = not available; PST = post-thrombotic syndrome; RCT = randomized controlled trial; Retro = retrospective; Pro = prospective.

Methods

In October 2022, an exhaustive search of pertinent literature was conducted primarily through PubMed, aiming to compare the outcomes associated with the utilization of anticoagulation alone vs the implementation of anticoagulation in conjunction with CDT. The search strategy encompassed the utilization of the following keywords: deep vein thrombosis, anticoagulants, catheter-directed thrombolysis, pharmacomechanical thrombectomy, and post-thrombotic syndrome. Additionally, we scrutinized the reference lists of retrieved studies to identify additional relevant articles, without imposing any temporal restrictions on the year of publication. The inclusion criteria encompassed research articles that compared the outcomes in a group receiving CDT plus anticoagulation with a control group receiving anticoagulation alone for the treatment of DVT. Conversely, the exclusion criteria entailed (1) review articles, and (2) research articles that examined the outcomes of only 1 modality of therapy for acute DVT. Data extraction was performed independently by the investigators for each article, including the first name of the author, patient characteristics in the control (anticoagulation) and experimental (CDT plus anticoagulation) groups, duration of follow-up, and respective primary and secondary outcomes. Additionally, mean age, percentage

of female patients, and study type were considered (**Table 1**). The primary outcomes encompassed the percentages of iliofemoral vein patency and PTS, while the secondary outcomes encompassed bleeding events, mortality, duration of hospital stay, and the risk of recurrent venous thromboembolism (**Table 2**).

Table 2. Primary and secondary outcomes of included research studies.

Study	Group	Iliofemoral patency	PTS	Bleeding	Death	PE	Hospital stay, days	Recurrent VTE
Young 2019[1]	CDT + AC	16 (94.1%)	NA	NA	Nil	NA	NA	NA
	AC	46 (86.5%)	NA	NA	Nil	NA	NA	NA
AbuRahma 2000[4]	CDT + AC	15 (83%)	4 (22%)	5 (23%)	Nil	1 (5%)	NA	NA
	AC	8 (24%)	23 (70%)	5 (15%)	Nil	Nil	NA	NA
Elsharawy 2001[5]	CDT + AC	13 (72%)	NA	NA	Nil	Nil	7	NA
	AC	2 (12%)	NA	NA	Nil	1 (6%)	5.5	NA
Riyaz 2014[6]	CDT + AC	NA	NA	177 (49%)	42 (1%)	642 (18%)	7.23 ± 5.8	NA
	AC	NA	NA	88 (24.5%)	31 (8%)	408 (11.4%)	5.02	NA
Enden 2012[7]	CDT + AC	58 (64%)	37 (41%)	20 (22%)	NA	NA	NA	10 (11%)
	AC	45 (45%)	55 (56%)	0	NA	NA	NA	18 (18%)
Lee[8]	CDT + AC	18 (66.6%)	5 (18.5%)	8 (29.6%)	NA	NA	NA	1 (3.7%)
	AC	10 (38.4%)	13 (50%)	5 (19.2%)	NA	NA	NA	2 (7.6%)
Enden 2009[9]	CDT + AC	32 (64%)	NA	10 (20%)	NA	NA	NA	NA
	AC	19 (35%)	NA	2 (4%)	NA	NA	NA	NA
Srinivas 2014[10]	CDT + AC	20 (71%)	5 (19%)	4 (15%)	2 (7%)	4 (15%)	5 ± 1.3	NA
	AC	7 (33%)	19 (68%)	Nil	2 (7%)	6 (21%)	4.8 ± 1.4	NA
Haig 2016[11]	CDT + AC	54 (79.1%)	37 (42.5%)	0	3 (3.4%)	NA	NA	13 (14.9%)
	AC	61 (70.9%)	63 (70.8%)	0	9 (10.1%)	NA	NA	21 (23.5%)

Zhang 2013[12]	CDT + AC	40 (85.1%)	18 (38.3%)	NA	NA	NA	NA	NA
	AC	56 (69.1%)	46 (56.8%)	NA	NA	NA	NA	NA
Haig 2014[13]	CDT + AC	68 (74.4%)	NA	3.0 (3.3%)	Nil	Nil	NA	10 (11%)
	AC	56 (59.6%)	NA	Nil	NA	NA	NA	18 (18%)
Notten 2020[14]	CDT + AC	NA	22 (28.5%)	4 (5.1%)	1 (1.2%)	Nil (0%)	NA	5 (6.4%)
	AC	NA	26 (26.6%)	Nil (0%)	3 (4%)	2 (2.6%)	NA	4 (5.3%)
Brailovsky 2020[15]	CDT + AC	NA	3 (0.2%)	58 (4.5%)	33 (2.6)	67 (5.2%)	6 (4-10)	154 (12)
	AC	NA	19 (1.5%)	39 (3%)	25 (1.9)	50 (3.9)	4 (2-7)	174 (13.5)
Kim 2016[16]	CDT + AC	NA	NA	1 (1.8%)	Nil	5 (8.9%)	10.76 ± 3.90	7 (12.5%)
	AC	NA	NA	Nil	Nil	10 (21.7%)	11.59 ± 9.34	3 (6.5%)
Alkhouli 2014[17]	CDT + AC	NA	NA	37 (6.5%)	11 (2%)	68 (12.1%)	8.1 ± 6.4	NA
	AC	BA	BA	32 (5.7%)	8 (1.4%)	44 (7.8)	6.9 ± 7.2	NA
Brailovsky 2014[18]	CDT + AC	NA	NA	NA	2.90%		9.97 ± 9.1	NA
	AC	NA	NA	NA	1.30%		6.83 ± 5.5	NA
Magnuson 2019[19]	CDT + AC	NA	NA	NA	NA	NA	6.4 ± 3.3	NA
	AC	NA	NA	NA	NA	NA	3.7	NA

CDT = Catheter-directed thrombolysis; AC = Anticoagulation; NA = Not available; PST = Post-thrombotic syndrome; VTE = venous thromboembolism.

The collected data were subjected to statistical analysis using SPSS Statistics (version 29.0) and Review Manager (version 5.1). Notably, most of the included studies predominantly featured female patients, constituting more than half of the study sample. During the data analysis process using Review Manager, fixed effects models were employed to represent the outcomes, specifically the secondary outcomes encompassing adverse events and duration of hospital stay. The statistical heterogeneity was assessed using the I^2 statistic, whereby values above or equal to 75% indicated high heterogeneity, values of 25% denoted low heterogeneity, and values of 50% signified moderate heterogeneity.

Results

The literature search identified a total of 64 full-text articles, of which 17 studies met the predetermined inclusion criteria and were thus selected for inclusion in the meta-analysis (**Table 1**). The data extracted from these 17 published articles encompassed a diverse range of study designs, including retrospective and prospective studies, as well as randomized clinical trials. The duration of follow-up varied among the included studies, with the shortest follow-up period being 6 months and the longest extending to 108 months, with an average follow-up duration of 33.1 months. Furthermore, the sample sizes in most of the studies were comparable between the 2 groups under investigation. However, the sample sizes ranged from relatively small, as observed in the study conducted by AbuRahma[4] and Elsharaw,[5] to quite substantial, reaching 3594 individuals in each group as reported by Riyaz.[6] It is worth noting that certain studies exhibited a female predominance, while others had a male predominance (**Table 1**). Moreover, the average age of the patients across all studies exceeded 39 years, with a mean age of 52.3 years.

Primary Outcomes

Ten studies[1,4,5,7-13] provided results regarding the percentage of iliofemoral vein patency. The results related to PTS were reported in 8 studies.[4,7,8,10-15] Through a meta-analysis, it was determined that compared with anticoagulants alone, the utilization of CDT was associated with a higher percentage of iliofemoral vein patency (95% confidence interval [CI] 1.78, 3.02; *P*<.00001; I^2 = 70%) and a reduced risk of PTS (95% CI 0.29, 0.51; *P*<.00001; I^2 = 55%). The number of patients in the anticoagulant group who achieved iliofemoral vein patency was lower compared with the CDT group. Furthermore, a lower incidence of PTS was observed in the CDT group compared with the anticoagulant group. Notably, when inputting the data into Review Manager, **Figure 1** and **Figure 2** revealed that increasing the sample size resulted in narrower confidence intervals. This observation explained the opposite movements of the CIs of patency and PTS (**Figure 1** and **Figure 2**). Heterogeneity was observed in PTS events (I^2 = 55%), which was resolved through a "leave-one-out meta-analysis" approach by excluding the study conducted by Notten et al in 2020.[14] Moreover, significant heterogeneity was identified in iliofemoral patency events (I^2 = 70%), which was addressed by excluding the study by Haig et al in 2016.[11]

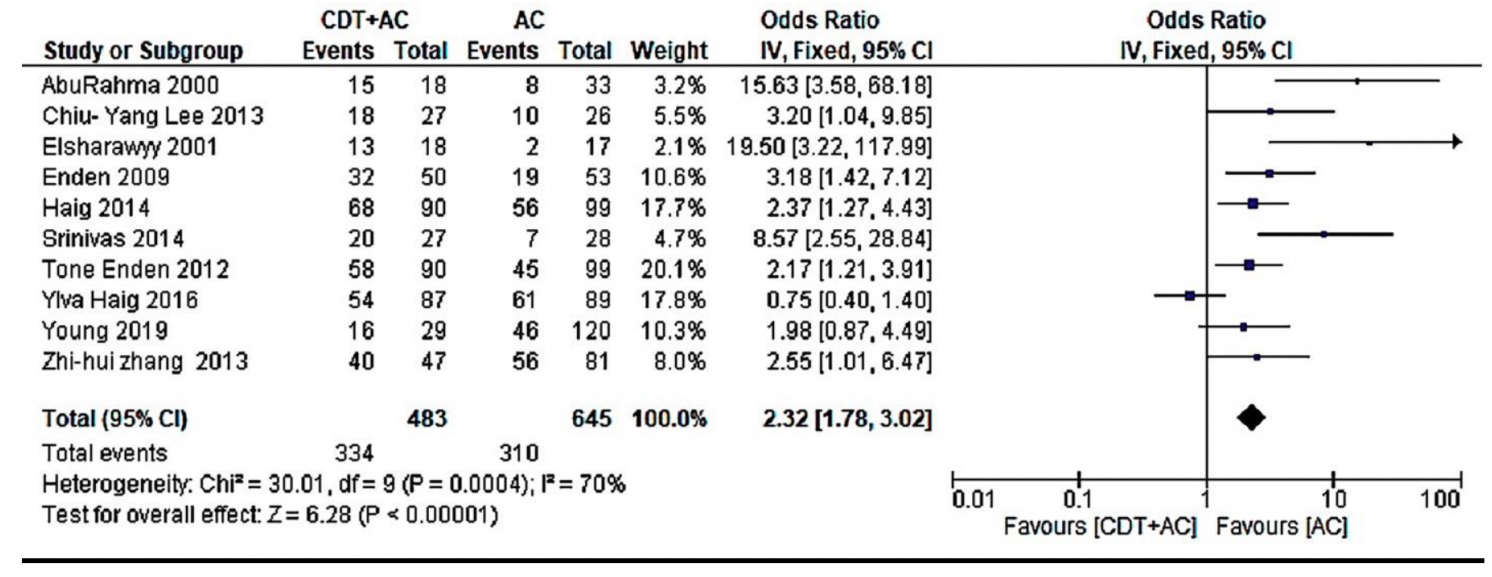

Figure 1. Meta-analysis of Iliofemoral patency (95% confidence interval 1.78, 3.02; *P*<.00001; I2 = 70%).

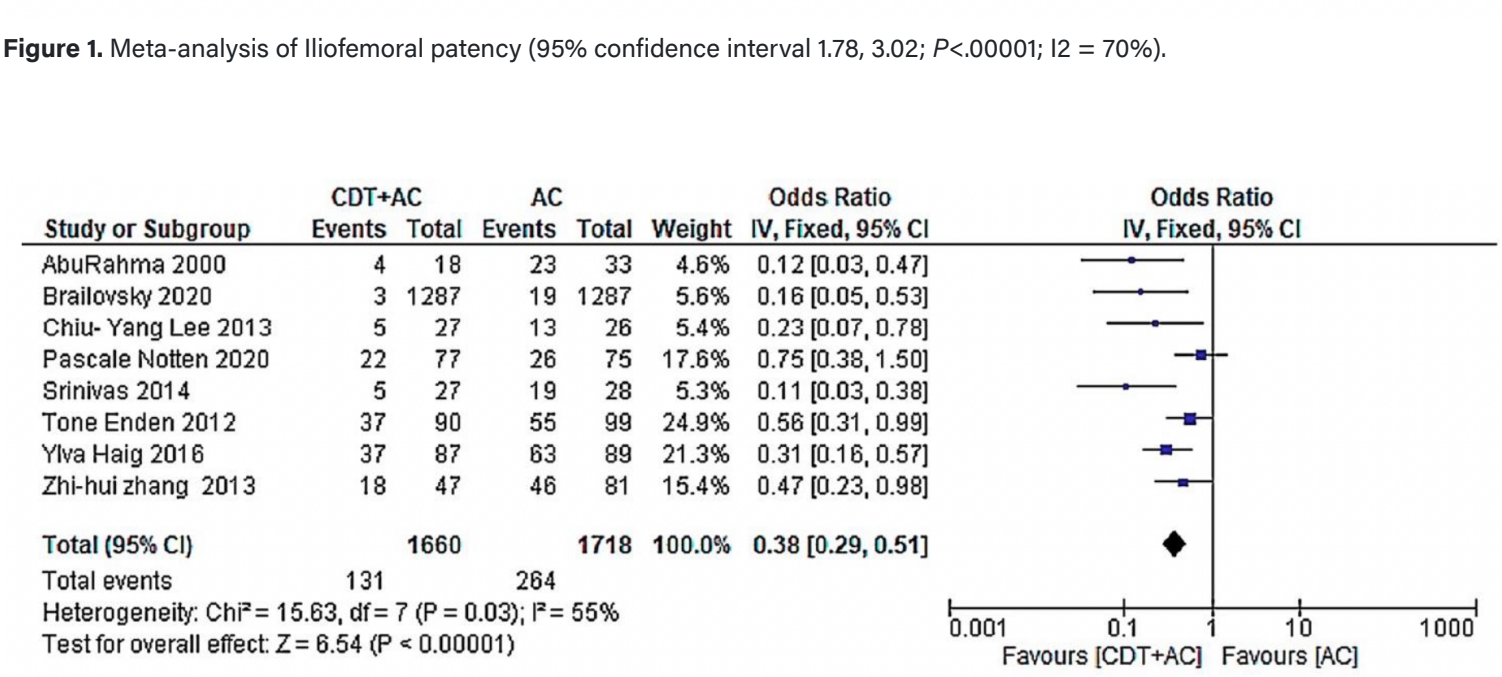

Figure 2. Meta-analysis of post-thrombotic syndrome (95% confidence interval 0.29, 0.51; *P*<.00001; I2 = 55%).

Secondary Outcomes

Information regarding bleeding occurrences was derived from 12 articles.[4,6-11,13-17] These studies indicate that CDT treatment increases the risk of bleeding (95% CI 1.53, 2.25; *P*<.00001; I^2 = 40%). Conversely, the use of anticoagulant therapy alone reduces the risk of bleeding (**Figure 3**), where both minor and significant bleeding events were counted as bleeding events.

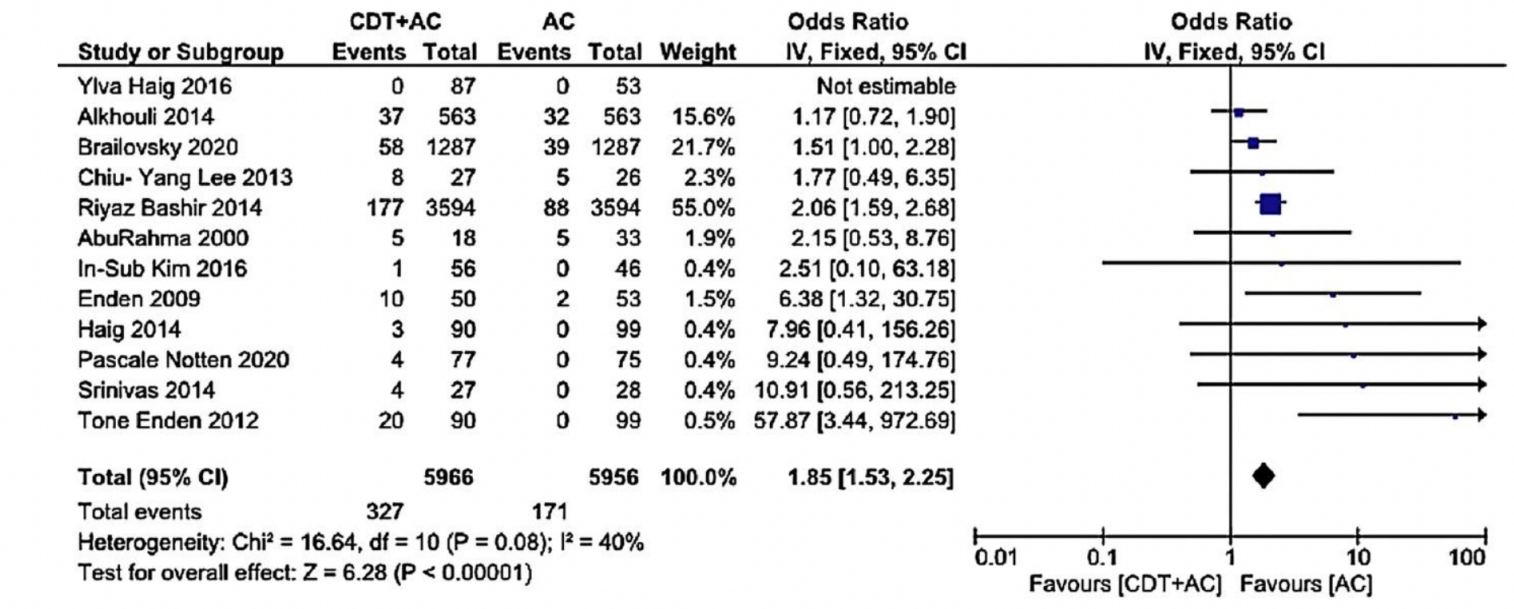

Figure 3. Meta-analysis of bleeding events (95% confidence interval 1.53, 2.25; *P*<.00001; I2 = 40%).

Data on deaths were documented in 12 studies.[1,4,5,6,10,11,13-18] These studies reveal that the incidence of death slightly increases with CDT compared with anticoagulant therapy, but there is no significant difference in the death rate between CDT and anticoagulation therapy alone (**Figure 4**) (95% CI 0.90, 1.63; $P = .20$; $I^2 = 43\%$).

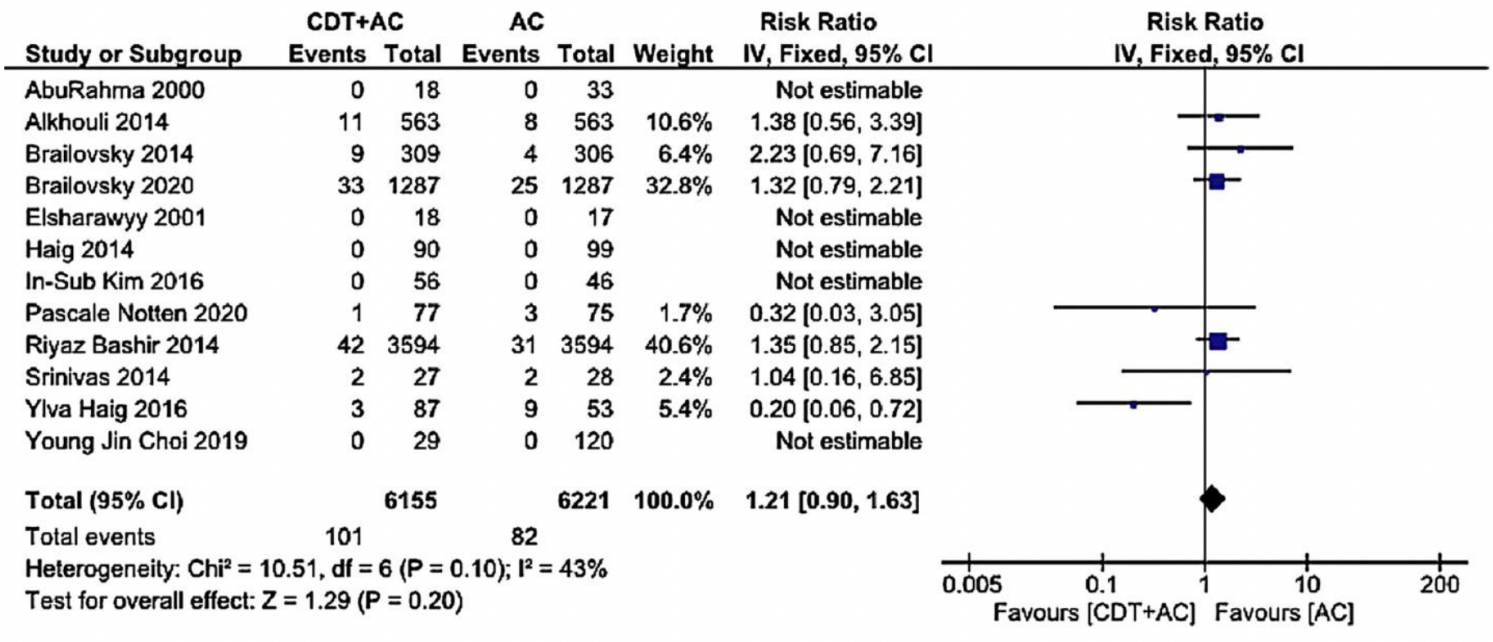

Figure 4. Meta-analysis of death events (95% confidence interval 0.90,1.63; *P* = .20; I2 = 43%).

Nine articles provided data on PE events,[4,5,6,10,13-17] indicating that treatment with CDT is associated with higher rates of PE events compared with anticoagulation treatment (95% CI 1.43, 1.81; *P*<.00001; $I^2 = 47\%$), despite a smaller number of patients receiving CDT in these studies compared with those receiving anticoagulation. The results display moderate heterogeneity ($30\% < I^2 < 60\%$) (**Figure 5**).

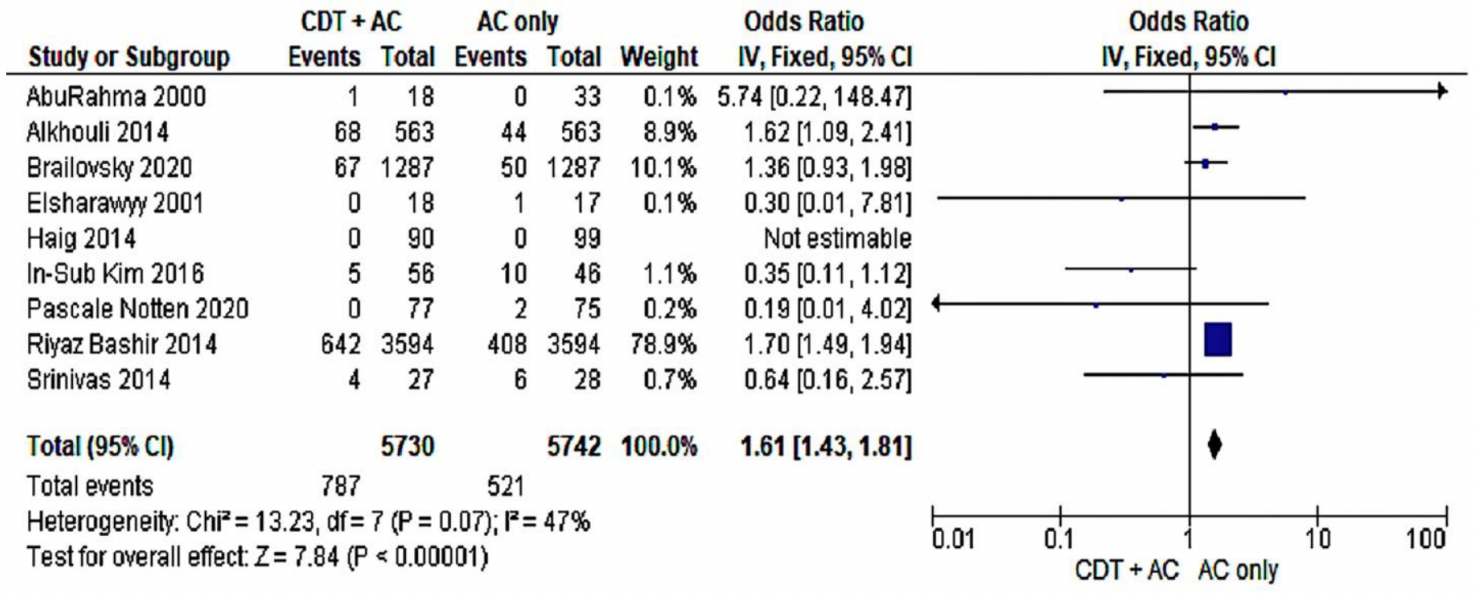

Figure 5. Meta-analysis of pulmonary embolism events (95% confidence interval 1.43,1.81; *P*<.00001; I2 = 47%).

Data concerning the duration of hospital stay were available from 8 studies.[5,6,10,15-19] They indicated a prolonged hospital stay with CDT compared with the anticoagulant group (95% CI 1.00, 2.23; *P*<.00001; $I^2 = 87\%$). This analysis shows significant heterogeneity ($75\% < I^2 < 100\%$) (**Figure 6**).

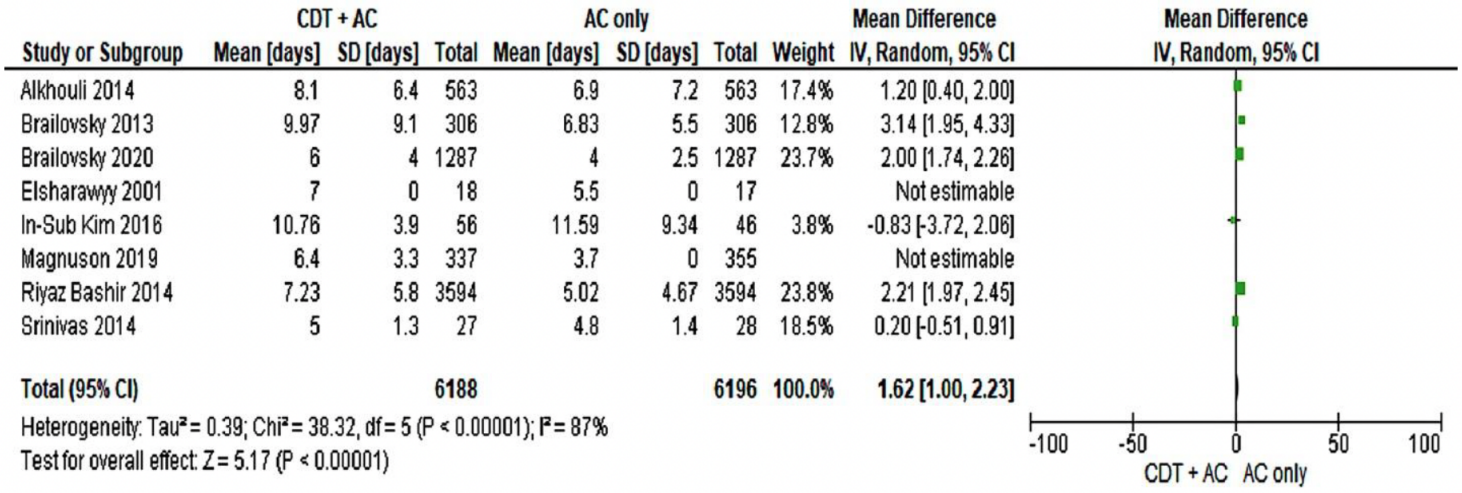

Figure 6. Meta-analysis of hospital stay duration (95% confidence interval 1.00, 2.23; *P*<.00001; I2 = 87%).

Statistical analysis of data on recurrent venous thromboembolism (VTE) events from 7 articles[7,8,11,13-16] (**Figure 7**) indicates a minimal decrease in recurrent VTE with CDT compared with anticoagulation; however, this difference was not statistically significant (95% CI 0.67, 1.00; $P = .05$; $I^2 = 0\%$).

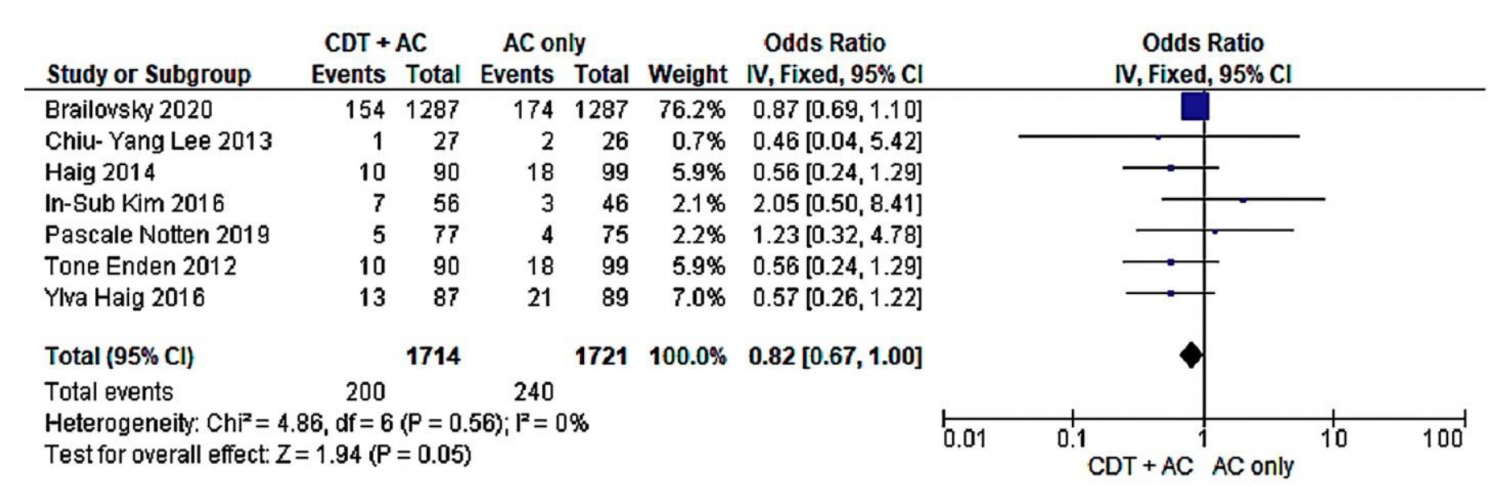

Figure 7. Meta-analysis of recurrent venous thromboembolism (95% confidence interval 0.67,1.00; *P* = 0.05; I2 = 0%).

Discussion

When comparing our meta-analysis with others in the literature, we found that our study encompassed more randomized controlled trials and featured a more extensive follow-up period. However, our current study aligns with other studies in demonstrating that CDT combined with anticoagulation proves to be an effective treatment modality for eliminating thrombus in patients with acute lower extremity DVT.[2] Similarly, Chang et al[3] conducted a systematic review and meta-analysis, which demonstrated that CDT yielded significantly better improvement in PTS compared with conventional anticoagulant therapy. Another meta-analysis conducted by Lu et al[20] highlighted the pivotal role of CDT in improving iliofemoral vein patency, albeit with an increased risk of bleeding, PE events, and prolonged hospital stay.

Primary Outcomes

Patients diagnosed with DVT who underwent anticoagulation therapy alone often experienced chronic venous dysfunction, as the anticipated dissolution of venous thrombus did not occur as expected.[21] Systemic thrombolytic therapy, which posed a significant risk of bleeding incidents and proved ineffective in eliminating thrombus, was subsequently discontinued.[22] In light of these limitations, CDT was developed as a targeted treatment approach specifically designed to dissolve thrombus in individuals with acute lower extremity DVT. The combination of CDT and anticoagulation therapy has demonstrated superior effectiveness in dissolving venous thrombus when compared with systemic thrombolytic therapy or anticoagulation therapy alone.[23] However, it is worth noting that despite the efficacy of CDT, current guidelines for acute proximal DVT of the leg still prefer anticoagulant therapy alone, although the quality of evidence supporting this preference is not robust (Grade 2C).[24,25] However, in the same guidelines the authors proposed that there is a subset of patients who may derive substantial benefits from CDT; these patients exhibit a strong preference for preventing PTS and assign a lower priority to the initial intricacies, costs, and bleeding risks associated with CDT. Among this group, the optimal proposed candidates for CDT possess iliofemoral DVT, symptoms of less than 14 days, favorable functional status, a life expectancy of at least 1 year, and a minimal risk of bleeding, in addition to patients facing impending venous gangrene.[24]

As a result, the use of CDT for acute lower extremity DVT remains a topic of ongoing debate. Recent years have witnessed several clinical studies investigating the effectiveness of CDT in this context.[26-29] To contribute to this body of research, our meta-analysis compared the outcomes of CDT plus anticoagulation therapy with anticoagulation therapy alone for the treatment of acute lower extremity DVT, drawing from a pool of 17 comparable studies. Among these studies, 10 examined the percentage patency of the iliofemoral vein.[1,4,5,7-13] The follow-up periods ranged from 6 months to 60 months, with varying durations

across the studies. Notably, the results indicated that the timely removal of thrombus through CDT during the acute phase can lead to improved flow and increased patency percentage of iliofemoral veins. Additionally, 8 studies[4,7,8,10-15] investigated the outcomes of PTS. These studies included follow-up periods ranging from 6 months to 9 years, with assessments conducted at various intervals. The findings revealed that CDT could significantly reduce the severity of PTS compared with anticoagulant therapy alone (95% CI 0.29, 0.51; $P<.00001$; $I^2 = 55\%$).

PTS, caused by venous outflow blockage, venous reflux, and calf muscle pump failure, often manifests as severe clinical symptoms such as venous ulcers, varicose veins, intractable edema, and chronic pain in the lower limbs.[30,31] Notably, iliofemoral DVT is a significant risk factor for the development of PTS, which significantly impairs the quality of life for affected individuals.[32,33] Thrombolysis therapy aims to mitigate PTS morbidity by effectively eliminating early thrombus, enhancing venous patency, preventing valvular incompetence, and potentially reducing the incidence of PTS.[34,35] However, the assignment of patients to this therapeutic modality did not yield superior improvements in their overall quality of life, and the assessment of quality-of-life scores using the evaluation scales did not reveal any notable disparities between the treatment groups in the CaVenT trial.[11] Thus, the debate surrounding the optimal use of CDT therapy for preventing PTS in the long term necessitates additional comprehensive research.

Secondary Outcomes

During the study, several complications were observed, including bleeding, PE, recurrent VTE events, and death.[20] Our meta-analysis revealed a significant association between CDT and a higher incidence of PE events ($P<.00001$, $I^2 = 47\%$), while recurrent VTE events did not show a significant difference between the CDT and anticoagulation groups ($P = .05$, $I^2 = 0\%$).

In a total of 9 studies[4,5,6,10,13-17] comprising 5730 patients in the CDT plus anticoagulation group and 5742 patients in the anticoagulation group, the number of PE events was 787 and 521, respectively. A statistically significant increase in PE events was observed in the CDT group (95% CI 1.43-1.81; $P<.00001$; $I^2 = 47\%$) with moderate heterogeneity ($30\%<I^2<60\%$). It should be noted that the Bashir et al study,[6] Brailovsky et al study,[15] and Alkhouli et al study[17] had larger sample sizes, which might have influenced the statistical results. Consequently, it is essential to consider preventive measures, such as vena cava filter implantation, to prevent PE during CDT or anticoagulation therapy.[20] The forest plot depicting pulmonary embolism events is displayed in **Figure 5**.

Regarding the duration of hospital stay, information was provided in 8 studiess5,6,10,15-19 involving 6188 patients in the CDT plus anticoagulation group and 6196 patients in the anticoagulation group. The hospital stay was significantly longer for patients receiving CDT than for those receiving anticoagulants alone (95% CI 1.00, 2.23; $P<.00001$; $I^2 = 87\%$), with considerable heterogeneity ($75\%<I^2<100\%$). The forest plot illustrating the duration of hospital stay is presented in **Figure 6**.

Additionally, 7 articles[7,8,11,13-16] provided information on recurrent VTE events, including 1714 patients in the CDT plus anticoagulation group and 1721 patients in the anticoagulation group. Among these patients, there were 201 recurrent VTE events in the CDT plus anticoagulation group and 240 in the anticoagulation group. No significant difference was observed between the 2 groups (95% CI 0.67, 1.00; $P = .05$; $I^2 = 0\%$). The forest plot representing recurrent VTE events is shown in **Figure 7**.

Our meta-analysis demonstrated increased bleeding events in patients undergoing CDT compared with those receiving anticoagulation therapy ($P<.00001$; $I^2 = 40\%$). The bleeding events ranged from minor to severe, with severe cases defined by a drop in hemoglobin levels of at least 2 g/dL, requiring more than 2 units of blood, or involving gastrointestinal or cerebral hemorrhage.[35] The fourth Cochrane Review update, which included 19 studies and 1943 patients, reported a higher rate of bleeding complications with CDT compared with anticoagulation therapy (CDT vs anticoagulation: 6.6% vs. 2.2%).[36] Most bleeding issues associated with CDT were related to the puncture site, and only a small number of cases had significant bleeding.[27,37] Advanced age, prolonged thrombolysis use, and procedural errors during CDT contribute to the increased risk of bleeding.[20] To mitigate the risk of bleeding, it is crucial to perform CDT procedures under the expertise of professional surgeons or interventional radiologists.[2,20] Utilizing ultrasound guidance to minimize multiple vessel punctures, as demonstrated in the Dumantepe et al study, can effectively decrease bleeding incidents during CDT.[38]

Twelve studies[1,4,5,6,10,11,13-18] included information on death events. Among them, the first 5 studies reported no deaths during follow-up. Four deaths were reported in the study by Notten et al, with 1 occurring in the CDT group and 3 in the anticoagulation group, but none were treatment related.[14] The remaining studies indicated that the mortality rate with CDT was slightly higher than with anticoagulation therapy, although the difference was not statistically significant.

This comprehensive analysis of secondary outcomes provides valuable insights into the efficacy and safety profiles of CDT and anticoagulation therapy. While CDT demonstrated a higher incidence of pulmonary embolism events and an increased risk of bleeding complications, it did not show a significant advantage in preventing recurrent VTE events compared with anticoagulation therapy alone. The findings underscore the importance of individualized treatment decisions, considering factors such as patient characteristics, bleeding risk, and the potential benefits of preventive measures. Limitations of this study includes the inclusion of nonrandomized controlled trials which may have affected the statistical outcomes. We also did not consider potential heterogeneity sources, which were variable between the studied outcomes. To address these limitations and strengthen statistical evidence, future trials including well-designed randomized controlled trials should aim for similar designs, minimizing heterogeneity for more convincing results.

Conclusion

This meta-analysis suggests that CDT can improve the patency of iliofemoral veins when compared with anticoagulation alone, leading to a reduction in PTS. However, it should be noted that the CDT group experienced a higher incidence of bleeding and PE events, as well as a longer average duration of hospital stay compared with the anticoagulation group. On the other hand, recurrent VTE and mortality rates did not significantly differ between the 2 groups. Therefore, the benefits and risks of CDT should be carefully weighed on a case-by-case basis with consideration of the patient's individual risk factors and preferences. ■

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