Published in final edited form as:

Pediatr Blood Cancer. 2020 February ; 67(2): e28057. doi:10.1002/pbc.28057.

The Association of Mediastinal Mass in the Formation of Thrombi in Pediatric Patients with Non-lymphoblastic Lymphomas

Jessica Gartrell, MD^{1,2}, Sue C. Kaste, DO^{2,3}, John T. Sandlund^{1,2}, Jamie Flerlage^{1,2}, Yinmei Zhou, MS⁴, Cheng Cheng, PhD⁴, Jeremie Estep, MD^{2,5}, Monika L. Metzger, MD, MSc^{1,2}

¹Department of Oncology, St Jude Children's Research Hospital, Memphis, TN

²University of Tennessee Health Science Center, Memphis, TN

³Department of Diagnostic Imaging, St Jude Children's Research Hospital, Memphis, TN

⁴Department of Biostatistics, St Jude Children's Research Hospital, Memphis, TN

⁵Department of Hematology, St Jude Children's Research Hospital, Memphis, TN

Abstract

BACKGROUND: Children diagnosed with cancer are at a significantly higher risk of developing a thrombotic event (TE) compared to the general population. The rarity of these events makes it difficult to discern the specific risk factors; however, age, sex, presence of central venous lines, inherited thrombophilia and mediastinal mass may play a role. The primary aim of this study is to identify prognostic characteristics of children diagnosed with non-lymphoblastic lymphomas associated with a greater risk of developing a thrombotic event early on in their disease, with an increased focus on mediastinal mass characteristics.

METHODS: Retrospective chart review of pediatric patients diagnosed with non-lymphoblastic lymphoma between 2004 and 2014 at St. Jude Children's Research Hospital.

RESULTS: TE occurred in 8.5% (n=28/330) of individuals at a median of 21 days from diagnosis of a non-lymphoblastic lymphoma, with 60% of TEs occurring within 30 days of diagnosis. Of the variables evaluated, only presence of a PICC [OR: 3.14 (95% CI: 1.24–7.98; p=0.02)] and degree of superior vena cava (SVC) compression of >25% increased the odds of developing a TE [OR: 2.2 (95% CI: 1.01–4.93; p=0.048)].

CONCLUSION: Pediatric patients with non-lymphoblastic lymphoma are at increased risk of developing TEs. In contrast to previous studies, presence of a mediastinal mass alone was not associated with a higher risk of TE, but individuals with a mediastinal mass with 25% or greater degree of SVC compression were more likely to develop a TE. This finding highlights a high-risk group of children that may benefit from prophylactic anticoagulation.

Corresponding Author: Monika Metzger, 262 Danny Thomas Place MS 721, Memphis TN 38105. P: 901-595-4974 F: 901-595-5319.

Conflicts of Interest

The authors declare there are no conflicts of interest.

Data availability statement: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Keywords

Pediatric hematology/oncology; hematology; hemostasis & thrombosis; Non-Hodgkin lymphoma; lymphoma

INTRODUCTION

Children diagnosed with cancer are 600 times more likely than healthy children to develop a thrombotic event (TE) [1, 2]. These events are frequently complicated by recurrent thrombi, post thrombotic syndrome, pulmonary emboli and death [3]. The rarity of these events in children with cancer make it difficult to discern the etiology of the events and thus preclude the ability to create evidence-based guidelines for thrombus prevention.

Literature to date has indicated that age, sex, presence of central venous line (CVL), inherited thrombophilia, and mediastinal mass may predispose pediatric patients to developing a thrombus [1, 3–8]. More specifically, the presence of a mediastinal mass has been found to be present in approximately 17% of patients with pediatric cancer and a thrombus [1, 2]; however, the mechanism behind this correlation is not completely understood. The thrombi can form anywhere in the body, but the majority are associated with a CVL and are found in the upper extremity [1, 2]. The primary aim of this study is to identify prognostic characteristics of children diagnosed with non-lymphoblastic lymphomas associated with a greater risk of developing a TE early on in their disease.

METHODS

Population

Patients under the age of 21 years diagnosed with non-lymphoblastic lymphoma at St Jude Children's Research Hospital between May 1, 2004 and April 30, 2014 were included in this retrospective study. Patients with lymphoblastic lymphoma were excluded because of their exposure to asparaginase, a known independent risk factor of thrombus formation [1, 2]. Furthermore, patients who were consult only, presented with relapsed disease, had lymphoma as a secondary malignancy, or had received therapy prior to arriving at St Jude were also excluded. The study was approved by our Institutional Review Board and data was managed according to HIPAA 2013.

Mediastinal masses and TE assessments

All patients treated had baseline imaging performed. The baseline diagnostic staging contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI) without and with intravenous administration of contrast, and posterior-anterior (PA) and lateral chest radiographs of each patient were reviewed by a single experienced radiologist (SCK) to determine the presence and characteristics of a mediastinal mass. A mediastinal mass was present if there was an alteration of the normal for age mediastinal contours on a chest radiograph or there was presence of otherwise unexpected lymphatic tissue on a chest CT or MRI. A mediastinal mass was considered bulky if the transthoracic ratio measured from the PA chest radiograph equaled or exceeded 33% and was calculated by dividing the maximum

transverse diameter of the mediastinum in centimeters (cm) by the maximum transverse diameter in cm of the chest at the dome of the diaphragm $\times 100$. We characterized mediastinal masses by CT or MRI as present or absent. When present, the area of the mass in cm^2 was estimated from the maximum transverse and maximum anteroposterior diameters of the mediastinal mass from the axial images. Further, we characterized the degree of compression of the superior vena cava (described in tertiles; $<25\%$, $25 - <50$ and $> 50\%$), presence or absence of compression of innominate and subclavian veins, the predominate side of the mediastinum occupied by the mass (right, left or central) and presence of collateral vessels, to verify the presence or absence of a thrombus.

Patients were coded as having a TE based upon the ultrasound with Doppler, CT, MRI or CT/MRI angiography imaging reports in the patient's medical record. Respective imaging was retrospectively reviewed for confirmation. Only TEs developed within the first 80 days from diagnosis were considered for this study. This range was chosen arbitrarily as it was felt that any TE developed within this timeframe was more likely to be associated with clinical factors present at diagnosis than with treatment related factors.

Data Collection

Following a comprehensive chart review, data collected for each participant included: demographics (age, gender, self-identified race and ethnicity), body mass index (BMI), obesity category (World Health Organization guidelines[9]), significant family history (stroke or thrombus in a first degree relative), type of lymphoma, inflammatory markers at diagnosis [C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)], coagulation work up (Factor V Leiden, protein C and S levels, anti-thrombin III (ATIII) and prothrombin gene mutation), central venous line type, CVL placement location (including side of body and vein placed), treatment given for the thrombus (tissue plasminogen factor (tPA), heparin therapy and/or line removal) and long term outcome data (presence of collateral vessels, limb swelling, etc.). The long-term outcome data, including swelling, pain and presence or absence of collateral vessels, was evaluated based on diagnostic imaging reports and clinic notes performed at their most recent clinic visit.

Statistical Analysis

Frequency tables and continuous summary statistics are presented for variables included in the analysis. Associations between categorical variables were evaluated using Pearson's Chi-square test or Fishers exact test, and continuous variables between groups were compared using the t-test. Logistic regression was also used to describe the relationships and to estimate the odd of developing a TE in other potential risk factors.

RESULTS

Participant and TE Characteristics

Over a 10-year period, a total of 355 individuals were diagnosed with primary non-lymphoblastic lymphoma at our institution; 330 participants met inclusion criteria (228 with Hodgkin and 102 with non-Hodgkin lymphomas) (Figure 1). TEs occurred in 8.5% ($n=28/330$) of individuals at a median of 21 days (range, 1 to 80 days) from diagnosis of

non-lymphoblastic lymphoma, with 60% of TEs occurring within 30 days of diagnosis (Figure 2). Nine patients were found to have a TE outside of 80 days with a mean of 634 days from diagnosis. Most participants (95%; n=312/330) had a CVL in place and 24/28 of TEs were CVL related. Age, gender, race, ethnicity, BMI, and obesity category of participants with and without a TE were similar (Table 1). A family history of thrombosis in a 1st degree relative or stroke was reported in 11.5% of participants and was not different between groups ($p = 0.8242$).

Clinical Presentation of TE

The non-Hodgkin subgroups treated included Burkitt (n=33), anaplastic large cell lymphoma (n=17), follicular lymphoma (n=7), nodal marginal zone (3), mediastinal large B-cell (n=8), primary cutaneous anaplastic large cell (n=2), mature B-cell NOS (n=32). A similar proportion ($p=0.780$) of participants with Hodgkin (8.7%) and non-Hodgkin lymphoma (7.8%) developed a TE. Three (11%) participants with TE had a concomitant pulmonary embolism (1/3 symptomatic). Most participants (79%; n=22/28) with a TE were symptomatic (arm swelling n=13, pain n= 10 and/or dyspnea= 1) at diagnosis of TE; 29% of the TEs (n=8/28) were found on diagnostic imaging performed at cancer staging with 6 of those patients being found on retrospective review. No patients with TE were documented as having superior vena cava syndrome. Inflammatory markers at diagnosis of lymphoma (ESR and CRP) were similar in participants with and without TE (Table 2).

None of the 15 participants with peripheral intravenous line developed a TE (Table 2). The odds of developing a TE were more than 3-fold higher in participants with a peripherally inserted central catheter (PICC) (78.6%) compared to those with a subcutaneous port (1%) or a Hickman (7%) line; specifically, the odds ratio (OR) was 3.14 (95% CI: 1.24–7.98; $p=0.02$). A similar proportion of participants had ipsilateral CVL placement with respect to the predominate side of the chest cavity occupied by a mediastinal mass.

In total, 57.9% of participants had a mediastinal mass at diagnosis of non-lymphoblastic lymphoma (Table 3). Of participants with a mediastinal mass, 10% (n=20/191) developed a TE; the odds of developing a TE were not increased (OR 1.9 [95% CI: 0.8–4.5] when a mediastinal mass was present at diagnosis. The size of the mediastinal mass, bulk of the disease, nor the predominate side of the mediastinum occupied by the mass increased the odds of developing a TE. In 25.8% (n=85/233) of participants there was compression of the SVC by >25%, and the odds for developing a TE when the SVC had this degree of compression was 2.2 (95% CI: 1.01–4.93; $p=0.048$).

Outcomes and interventions of Patients with a TE

Tissue plasminogen activator (tPA) was administered as flushes through the line to 39% (n=11/28) of participants who developed a TE and 46% (n=13/28) underwent removal of their CVL as a direct result of the TE (Table 4). No patients required systemic tPA. Thrombectomy was performed in one patient and an inferior vena cava filter was placed in another patient. Low molecular weight heparin therapy was used in 68% of patients for a median time of 133.5 days (range, 18 to 753 days). At long term follow up, averaging 25

months, imaging demonstrated development of collateral veins in 39% of patients and 4% had arm swelling. Nobody developed a second TE.

Coagulation work-up in patients with TE

Of the 21 patients who had coagulation work up performed, four were found to have lupus anticoagulant, one was found to have protein C deficiency. There was no patient found to have Factor V Leiden, Protein S or ATIII deficiency or a prothrombin gene mutation.

DISCUSSION

In this retrospective study, 8% of children with newly diagnosed non-lymphoblastic lymphoma developed a TE within 80 days of diagnosis, and likely represents the most accurate published estimate of prevalence in this population, where the reported prevalence of TE complications in pediatric patients with lymphoma ranges from 7.7 – 21% [1–3, 6, 7]. In our study, 9 TEs which were diagnosed outside of the 80-day window, with a mean of 634 days from diagnosis. We feel these TEs are more likely related to the treatment and complications than the initial presentation of a mediastinal mass. The majority of published studies include patients with lymphoblastic lymphoma who are treated with pegylated asparaginase, a known risk factor for TE, and likely overestimate the prevalence of TE for children with newly diagnosed non-lymphoblastic lymphoma [1, 2]. It is important to note that 29% of patients who had TE, had it at the time of presentation on routine imaging. Further, in 6/8 of these patients the thrombus was found in retrospective review of the imaging, highlighting the importance of educating physicians and radiologist to have heightened awareness for TE in this population.

Previous studies have reported that children with malignancy over the age of 9 or 12 years have a significantly higher risk for developing a TE [1, 2, 4, 7, 8, 10]. Our analysis showed a trend in the same direction; however, the influence of age did not reach statistical significance. This is likely due to the fact that the majority of our patients were older than 9 years of age given the adolescent and young adult prevalence of Hodgkin lymphoma. BMI also trended toward statistical significance ($p=0.06$); however, the clinical significance is less striking, with means of 21.8 kg/m^2 and 24.1 kg/m^2 in those without and with thrombus, respectively. To further evaluate the clinical significance of BMI, we evaluated whether being obese vs not obese was a risk factor. This did not reach statistical significance ($p=0.11$). Similar to other studies, race, ethnicity and gender played no significant role in the development of a TE.

We found that the presence of a mediastinal mass alone was not a statistically significant risk factor for the development of a TE in our patient cohort [1, 2, 7], however, greater than 25% SVC compression was found to be significant. This association suggests that it is not the presence of a mediastinal mass alone that puts a patient at risk but instead the degree of compression the mass causes on the SVC. This is the first study to evaluate the degree of SVC compression and sheds new light on further defining who may benefit from prophylactic anticoagulation therapy.

The mechanism of TE in malignancy is not entirely understood. People have implicated the inflammatory state that is seen in this population while others believe that the development of TE is more of a mechanical issue (1). In our analysis the inflammatory markers analyzed did not identify a group at higher risk. However, these markers were not consistently obtained. The degree of SVC compression did reach statistical significance suggesting that mechanical issues play a role and may be a nidus for the development of TEs in this patient population as compression on the SVC may alter normal laminar blood flow and velocity.

The role of CVLs is difficult to assess as the majority of our patients received a CVL to support treatment. None of the 8 patients without a central line developed a thrombus. Patients who received a PICC line were more likely to develop a thrombus ($p=0.04$). However, this data may be biased in that most patients who have a large mediastinal mass at diagnosis are not stable for sedation due to concern for airway compromise during anesthesia and, therefore, initially receive a PICC line instead of a subcutaneous port or Hickman line. In the case of Hodgkin lymphoma patients, all therapy is routinely administered through a PICC line.

CVLs are typically placed prior to starting chemotherapy in order to administer the agents necessary. Our data suggests that this may place patients at higher risk of TE and so strategies to avoid CVL placement need to be considered to lessen this risk. Contrary to a prior study that suggested that left sided lines were associated with a higher risk, we found no association between the side of the central line and the development of a TE [5]. This study also suggested that line associated thrombi may also be related to surgical technique, a factor we did not evaluate. CVLs at our institution are cared for using a uniform CVL standard of practice, where central lines are flushed with heparinized saline on a regular basis. Therefore, the care of the CVL was standardized and likely not contributory.

The results of our study must be considered in light of its strengths and weaknesses. It is a well characterized single institution population with patients receiving standardized therapies. This is the first study to further define characteristics of the mediastinal mass itself, shedding light on the possible pathogenesis of TE in this population. All imaging was reviewed by a single pediatric oncologic radiologist (SCK) with more than 27 years of experience who consistently defined the presence or absence, size and configuration of mediastinal mass and confirmed the presence or absence of a thrombus. This study is limited by the retrospective design. Hypercoagulation studies as well as inflammatory markers, which have been shown to be relevant to the development of TEs, were not consistently obtained. Lack of standardization of imaging and the decision to image when symptomatic was provider dependent and therefore the incidence of TE may be underestimated. Similarly, decisions were made on a case-by-case basis regarding therapy for TE and whether or not to remove a CVL.

Conclusion

Thromboembolic events are rare in the pediatric population; however, the risk is higher in children undergoing treatment for malignancy. In our single institution study, 8% of patients presenting with non-lymphoblastic lymphoma were found to develop TE in the first 80 days from diagnosis, with a third of those patients being present at diagnosis. In contrast to

previous studies, presence of a mediastinal mass alone was not associated with a higher risk of TE; however, the risk of TE was increased if the mass was causing greater than 25% SVC compression. Those who develop a TE may be subjected to line removal and undertake the risks of low molecular weight heparin therapy. Patients with TEs have increased morbidity with pain and swelling and are at risk of TE associated mortality. Our findings suggest that newly diagnosed patients with greater than 25% SVC compression should be considered high risk for thrombus formation and the presence of CVL may increase that risk. Therefore, efforts to avoid immediate CVL placement should be considered until the compression can be resolved. Further, this points to a high-risk group that anticoagulation may be beneficial for and should strongly be considered especially if a CVL must be placed. Those with large masses without SVC compression appear to be at lower risk so efforts should be made to limit unnecessary exposure to anticoagulation therapy for this population. Future prospective studies should evaluate the safety and efficacy of prophylaxis in this population.

Abbreviation Term

ATIII	anti-thrombin III
BMI	body mass index
CRP	c-reactive protein
CT	contrast-enhanced computed tomography
CVL	central venous line
ESR	erythrocyte sedimentation rate
MRI	magnetic resonance imaging
OR	odds ratio
PA	posterior-anterior
PICC	peripherally inserted central catheter
PIV	peripheral intravenous catheter
SVC	superior vena cava
TE	Thrombotic event
tPA	tissue plasminogen factor

References

1. Athale U, et al., Epidemiology and clinical risk factors predisposing to thromboembolism in children with cancer. *Pediatr Blood Cancer*, 2008 51(6): p. 792–7. [PubMed: 18798556]
2. Athale UH, et al., Thromboembolism in children with lymphoma. *Thromb Res*, 2008 122(4): p. 459–65. [PubMed: 18237767]
3. Wiernikowski JT and Athale UH, Thromboembolic complications in children with cancer. *Thromb Res*, 2006 118(1): p. 137–52. [PubMed: 16039698]

4. Lipay NV, Zmitrovich AI, and Aleinikova OV, Epidemiology of venous thromboembolism in children with malignant diseases: a single-center study of the Belarusian Center for Pediatric Oncology and Hematology. *Thromb Res*, 2011 128(2): p. 130–4. [PubMed: 21492908]
5. Male C, et al., Central venous line-related thrombosis in children: association with central venous line location and insertion technique. *Blood*, 2003 101(11): p. 4273–8. [PubMed: 12560228]
6. O'Brien SH, et al., Venous thromboembolism and adolescent and young adult oncology inpatients in US children's hospitals, 2001 to 2008. *J Pediatr*, 2011 159(1): p. 133–7. [PubMed: 21353248]
7. Schonning A, et al., Venous thrombosis in children and adolescents with Hodgkin lymphoma in Sweden. *Thromb Res*, 2017 152: p. 64–68. [PubMed: 28249199]
8. Putti MC and Randi ML, Thrombotic complications in children with haematologic malignancies. *Thromb Res*, 2010 125 Suppl 2: p. S151–4. [PubMed: 20433996]
9. de Onis M and Lobstein T, Defining obesity risk status in the general childhood population: which cut-offs should we use? *Int J Pediatr Obes*, 2010 5(6): p. 458–60. [PubMed: 20233144]
10. Ko RH and Thornburg CD, Venous Thromboembolism in Children with Cancer and Blood Disorders. *Front Pediatr*, 2017 5: p. 12. [PubMed: 28220143]

TE, Thrombotic event

Figure 1:
Flow diagram of evaluated patients

Figure 2:
Days from diagnosis of lymphoma to time of thrombotic event

TABLE 1

Characteristics of participants with and without a thromboembolism

Variable	All patients	Patients without TE	Patients with TE	P value
Total	330	302	28	
Age at diagnosis				
Mean	13.7	13.6	15.1	0.06
SD	4.4	4.4	4.0	
Gender [n (%)]				
Male	185 (56.1)	173 (57.3)	12 (42.9)	0.14
Female	145 (43.9)	129 (42.7)	16 (57.1)	
Race [n (%)]				
White	212 (64.2)	195 (64.6)	17 (60.7)	0.82
Black	102 (30.9)	92 (30.5)	10 (35.7)	
Other	16 (4.8)	15 (5.0)	1 (3.6)	
BMI at Diagnosis				
Mean	22.0	21.8	24.1	0.06
Std	6.2	6.1	7.0	
Median	21.0	21.0	22.0	
Minimum	11.9	12.6	11.9	
Maximum	51.1	51.1	39.9	
<u>BMI Category</u> *				
Obese	56 (17.0)	48 (15.9)	8 (28.6)	0.11
Not obese	274 (83.0)	254 (84.1)	20 (71.4)	

* Defined by World Health Organization Guidelines

TE, thromboembolism; SD, standard deviation; BMI, body mass index;

TABLE 2

Characteristics of clinical presentation and diagnosis of lymphoma

Variable	All patients	Patients without TE	Patients with TE	P values
Total	330	302	28	
ESR at Diagnosis				
Median	27.0	27.0	41.0	0.80
Minimum	0.0	0.0	3.0	
Maximum	134.0	134.0	119.0	
CRP at diagnosis (mg/dL)				
Median	2.1	1.9	3.5	0.40
Minimum	0.0	0.0	0.0	
Maximum	30.2	30.2	23.6	
Line placed [n (%)]				
PICC	175 (53.0)	153 (50.7)	22 (78.6)	0.04*
PIV	70 (21.2)	66 (21.9)	4 (1.0)	
SQP	67 (20.3)	65 (21.5)	2 (7.0)	0 (0.0)
Hickman	15 (4.5)	3 (1.0)	0 (0.0)	
Unknown	3 (0.9)			

TE, thromboembolism; ESR, erythrocyte sedimentation rate; CRP C-reactive protein; PICC, peripheral intravenous central catheter; PIV, peripheral intravenous line; SQP, subcutaneous port

TABLE 3

Characteristics of the mediastinal mass

Variable	All patients	Patients without TE	Patients with TE	P value
Total	330	302	28	
Mediastinal Mass				
No	138 (41.8)	130 (43.0)	8 (28.6)	0.13
Yes	191 (57.9)	171 (56.3)	20 (71.4)	
Unknown	1 (0.3)	1 (0.3)	0 (0.0)	
Bulky Mediastinum				
Yes	98 (29.7)	86 (28.5)	12 (42.9)	0.13
No	226 (68.5)	210 (69.5)	16 (57.1)	
Unknown	6 (1.8)	6 (2.0)	0 (0)	
Mediastinal mass (cm ²)				
Median		55.50	76.49	0.25
Minimum		0.78	2.24	
Maximum		216.00	177.00	
Site of Bulk				
Right	48 (14.5)	44 (14.6)	4 (14.3)	0.40
Left	53 (16.1)	48 (15.9)	5 (17.9)	
Midline	90 (27.3)	79 (26.2)	11 (39.3)	
Unknown	1 (0.3)	1 (0.3)	0 (0.0)	
No Mass	138 (41.8)	130 (43.0)	8 (28.6)	
CVL on Same Side of Mass				
Yes	46 (13.9)	40 (13.2)	6 (21.4)	0.18
No	55 (16.7)	52 (17.2)	3 (10.7)	
N/A ^a	229 (69.4)	210 (69.5)	19 (67.9)	
SVC Compression [n (%)]				
0–24.9%	233 (70.6)	217 (71.9)	16 (57.1)	0.05 [*]
>25%	85 (25.8)	73 (24.2)	12 (42.9)	
Unknown	12 (3.6)	12 (4.0)	0 (0.0)	

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Bulky disease based on a transthoracic ratio% greater than or equal to 33.
*
^ includes patients without a mass or those whose mass was defined as midline
CVL, central venous line; SVC, superior vena cava

TABLE 4

Outcomes and interventions of patients with TE

Number of TE events	28 (%)
Pulmonary embolism present [n (%)]	
Yes	3 (11)
No	25 (89)
Days from Diagnosis of Lymphoma to TE	
Mean	27
Median	21
Std	25
Minimum	1
Maximum	80
TPA Used [n (%)]	
Yes	11 (39)
No	10 (36)
Unknown	7 (25)
Average number of TPA flushes (# of doses)	1.04
Minimum	0
Maximum	4
Line Removed [n (%)]	
Yes	13 (46)
No	11 (39)
N/A: thrombus not line associated	4 (14)
LMWH Used	
Yes	19 (68)
No	9 (32)
# Weeks of LMWH Used	
Mean	23
Minimum	0
Maximum	107
Collaterals present at long term follow up [n (%)] *	

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Number of TE events		28 (%)
Yes		11 (44)
No		14(56)
Arm swelling present at follow up [n (%)] *		
Yes		1 (4)
No		24 (96)

* patients with PE were excluded

TE, thromboembolism; TPA, tissue plasminogen activator; LMWH, low molecular weight heparin