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## ORIGINAL ARTICLE

**Title:** Impact of multidisciplinary team meetings on the management of venous thromboembolism. A clinical study of 142 cases

**Short title:** Impact of multidisciplinary team meetings on the management of VTE

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## ABSTRACT

**Objective.** Numerous guidelines have been published on the management of venous thromboembolism (VTE). However, therapeutic decision-making may prove challenging in routine clinical practice. With this in mind, multidisciplinary team (MDT) meetings have been set up in Rennes University Hospital, France. This study sought to describe the situations discussed during MDT meetings and to assess whether the meetings bring about changes in the management of these patients.

**Materials and methods.** A retrospective single-center study conducted at the Rennes University Hospital included cases presented from the beginning of the MDT meetings (February 2015) up to May 2017.

**Results.** In total, 142 cases were presented in 15 MDT meetings, corresponding to a mean of  $10 \pm 4$  cases per meeting. Of these, 129 related to VTE patients: 33 provoked VTEs, 22 unprovoked VTEs, 40 cancer-related VTEs, and 25 unspecified VTEs. MDT meetings led to significant changes in the anticoagulation type (therapeutic, prophylactic, or discontinuation) and duration, but not in the anticoagulant choice (direct oral anticoagulants, vitamin K antagonists, heparins, etc.).

**Conclusion.** Requests for MDT meetings are made for all VTE types, and these meetings have an impact on VTE management.

**Keywords:** Venous thromboembolism disease; Multidisciplinary Evaluation Consortium; Anticoagulation; Cancer

## INTRODUCTION:

Over recent years, a number of advances in the epidemiology, diagnosis, and treatment of venous thromboembolism (VTE) have changed how patients with VTE are managed. The most significant changes have related to the 1) assessment of the risk of recurrence, 2) duration of anticoagulation, and 3) dosage regimens. With regard to the risk of recurrence, several randomized studies have shown that initial VTEs recur according to the same phenotype and same mechanism – *i.e.*, a pulmonary embolism recurs as a pulmonary embolism, and unprovoked VTE recurs in an unprovoked manner (3,4). Meanwhile, a recent update of major and minor provoking factors has been proposed by the International Society of Thrombosis and Haemostasis, which facilitates the gauging of recurrence risk (5,6). The concept of modulating

factors has emerged, with some factors indicating that treatment should be stopped and others that it should be extended. These latter include major thrombophilia, the presence of a vena cava filter, chronic inflammatory disease, and patient preference. As regards the duration of anticoagulation, in the PADIS-EP study of a vitamin K antagonist (VKA) for 24 months *versus* 6 months followed by placebo, the benefit of extended treatment disappeared after treatment was stopped (4). That study gave rise to the concept of "long-term" treatment for idiopathic pulmonary embolism. The AMPLIFY-EXT and EINSTEIN CHOICE studies, meanwhile, investigated the possibility of low-dose long-term treatment with direct oral anticoagulants (DOAs) (7,8).

In France, VTE is managed by physicians from different specialties working in public and private hospitals as well as in private practice. To harmonize practices regardless of where physicians work, numerous guidelines have been published (9,10). These guidelines facilitate decision-making in many settings, but some situations are more complex with regard to diagnosis and/or treatment, particularly when the bleeding risk is high. It is in such situations that multidisciplinary team (MDT) meetings come into their own (11). These discussions involving specialists from different backgrounds (the oncologist in particular) result in consensus-based decisions that take a greater number of parameters into consideration. MDT meetings on thrombosis and antithrombotics were set up in our institution along the lines of those established in oncology. This study aimed to describe the characteristics of the situations discussed during these MDT meetings and to gauge the impact of these meetings on the management of VTE patients.

## MATERIALS AND METHODS:

### Setting up the MDT meetings:

MDT meetings on thrombosis and antithrombotic management were set up in February 2015 in Rennes University Hospital, France. The idea is to discuss the diagnostic and therapeutic management of patients with arterial and venous thrombosis. The specialties represented are: hemostasis, internal medicine, oncology, geriatrics, vascular medicine and radiology. These meetings are also open to practitioners from outside the University Hospital, including general hospitals, private practitioners, and vascular specialists. All cases presented are recorded. An information sheet is completed by the referring physician, including the following items: date of the MDT meeting, patient's surname, patient's first name, date of birth, case presented by, diagnosis and problem, findings of the oncology MDT meeting if patient has a neoplastic disease, VTE diagnosis, kidney function (clearance in mL/min, with the calculation method specified), and question(s) asked. The case is presented by the referring physician and the names of the physicians in attendance are recorded. The committee determines how often meetings are to be held and draws up a provisional timetable. A treatment plan is suggested at the end of the meeting.

**Study design and objectives:** This was a descriptive retrospective single-center study conducted in Rennes University Hospital. No consent was required since the study was conducted as part of an investigation of current practices.

The study's primary objective was to provide an overview of the cases presented at MDT meetings over the 3 years of their existence. The secondary objective was to assess what changes resulting from MDT meetings had been made for the treatment of VTE patients with regard to anticoagulation (none, prophylactic, therapeutic, or discontinuation), choice of anticoagulant (heparin, DOA, VKA, etc.), and duration of anticoagulation depending on whether the VTE was provoked, unprovoked, or cancer-related. To investigate the difference between the initial management and that proposed in the thrombosis MDT meeting, we had to exclude a group of patients because the provoked, unprovoked, or cancer-related nature of their VTE was unspecified due to a lack of information.

**Data analysis:** All information in the MDT sheets was collected anonymously and then collated in an Epi Info™ database and analyzed in Excel®. The answers were expressed as a number and a percentage. Fisher's test was used to determine whether results were statistically significant, with a p value < 0.05 considered statistically significant.

## RESULTS:

A total of 142 cases were presented in 15 meetings between February 2015 and May 2017. The mean was  $10 \pm 4$  cases per meeting. Of those 142 cases, 13 were excluded because they related to isolated arterial disease only, whereas 129 related to VTE patients (Figure 1). Of the 129 information sheets completed, at least 43 (33%) were incomplete, with information on kidney function missing in particular. The date of birth was missing in 10 sheets (8%).

Characteristics of the VTE patients presented during the MDT meetings:

The mean age of our population was  $52 \pm 19$  years and ranged between 6 and 85 years. Most were women (n=75; 58%). Personal medical history was provided for 113 patients (87%) and family history for 32 patients (24.8%). The characteristics are presented in Table 1.

Regarding provoked VTE cases (n=33), the triggering factors were, in descending order of frequency: acute medical condition/bed rest/hospitalization for less than 3 months (n=13), pregnancy or postpartum (n=8), combined oral contraceptive pill (n=8), travel for more than 6 hours (n=8), major surgery within the previous 3 months (n=6), and multiple trauma or trauma to the lower extremities requiring immobilization for 3 months (n=1). It should be noted that in a number of cases, there existed several triggering factors.

As regards cancer-related VTE cases (n=49), the three main neoplastic conditions among the patients were breast cancer (43%), ovarian cancer (23%), and colorectal cancer (14%).

In 54 cases of the population (42%), a thrombophilia workup was ordered before an MDT decision was made. The workup was complete and normal in 12 cases (9.3%), and complete and abnormal in 23 (17.8%) (12).

Reasons for requesting an MDT meeting

Six reasons for requesting meetings were uncovered. These related to whether anticoagulation was indicated (n=53; 41%), to the duration of anticoagulation (n=46; 35.6%), or more broadly to the overall therapeutic management of a patient in terms of anticoagulation and/or other treatments (n=12; 9.3%). There were also questions about the feasibility of discontinuing anticoagulation (n=8; 6.2%), the choice of anticoagulant (n=5; 3.8%), and the need for clinical or paraclinical testing (thrombophilia workup or imaging) to supplement diagnosis (n=5; 3.8%). In addition to the six main reasons, questions about removing or placing a vena cava filter were also raised eight times in the 129 cases included (6.2%).

Impact of the MDT meetings.

We were able to analyze 104 cases (80%). On analysis of the results, it became apparent that three main categories of therapeutic decisions were made. They concerned the type of anticoagulation (none, prophylactic, therapeutic, discontinuation (i.e/stop)), choice of

anticoagulant (heparin, VKA, DOA, not specified), and duration of anticoagulation (short, extended, not specified).

Type of anticoagulation:

There was a significant difference between the initial treatment and the one suggested in the MDT meetings in the 104 patients (Table 2). The difference was significant in the three groups: provoked, unprovoked and cancer-related VTE groups. MDT meetings led to the discontinuation of 18 anticoagulation treatments. It was not possible to analyze changes in dosage regimens as a result of the MDT meetings owing to a lack of data.

Choice of anticoagulant:

No significant difference was found in the choice of anticoagulant before and after the MDT meetings. It is worth noting that there was an increase in the initiation of DOAs in patients with cancer-related VTE after the MDT meetings (Table 3).

Duration of anticoagulation:

There was a significant difference between the duration of anticoagulation initially recommended and that chosen in the MDT meetings, which favored a significantly longer treatment than the initial one (Table 4).

## DISCUSSION:

This original study revealed that 1) the number of challenging cases on VTE management is significant in clinical practice 2) these difficulties apply to the three types of VTE (provoked, unprovoked, and cancer-related), and 3) the MDT meetings significantly changed patient management with regard to the type and duration of anticoagulation.

Around 10 cases were discussed per meeting even though our MDT meetings had not at all been "advertised" in our institution. Generally, the number of cases discussed varied between 6 and 17, and it has been constantly rising. This forced us to increase the frequency of our meetings, which were held once every 6 to 8 weeks at the beginning, and which are now held once every 4 weeks. Before organizing things this way, opinions were given by different doctors, and this may have limited standardized management. With things organized this way, multidisciplinary discussion harmonizes the decisions and makes it easier for doctors from outside our center to request an opinion. This also helps to bring teams from different centers together and to foster ties between hospital- and community-based practitioners. However,

due to a lack of standardization, it cannot be said with any certainty that all decisions made in the MDT meetings were passed on to the family physicians.

Contrary to popular belief, unprovoked VTE cases are not the only ones that cause problems (13). Although the management of provoked VTE appears to be more standardized (9), 26% of the requests for meetings were related to this indication, showing that even this setting may be challenging for physicians in every day practice. On the other hand, it is not surprising to see that most requests (38%) concerned patients with cancer-related VTE, since cancer raises many questions: is the cancer active, what is the patient's bleeding risk and what quality of life can be expected? Indeed, on that score, our study revealed that although DOAs were not yet indicated for cancer-related VTE, the MDT meetings decided to suggest treating some patients (n=12) off-label with this type of anticoagulants, mostly for the patient's quality of life (14).

There was a significant difference in the type and duration of anticoagulation between initial management and that proposed in the MDT meetings, although this difference was not observed with regard to the choice of anticoagulant. The decisions made in the MDT meetings did therefore significantly change patient management. Nearly 20% of cases led to the discontinuation of anticoagulation deemed unnecessary. That said, it was impossible to gauge whether or not these changes in management were beneficial. A registry could be set up to evaluate whether any long-term benefit exists.

Another important point raised by our study is off-label use. In unusual, complex cases, one of the roles of MDT meetings is to be able to tailor the application of good clinical practice in compliance with international guidelines on standards of care. For example, in cancer-related VTE, the adherence of patients to anticoagulation with low-molecular-weight heparin (*i.e.*, injections) becomes increasingly difficult. In such cases, once consensus has been reached, prescribing another form of anticoagulation may be considered. That is why in 12 cases (25%) of the cancer-related VTE group, DOAs were prescribed instead of low-molecular-weight heparin. However, it was very difficult to ascertain whether off-label treatments were prescribed in the provoked and unprovoked VTE groups (7,10). Since January 2018, off-label use of rivaroxaban has been allowed, with the responsibility for the decision lying with the physician (see Transparency Committee of the Haute Autorité de Santé, the French health authority, January 2018).

Regarding the limitations of our study, the first bias that needs to be considered is an interpretive bias. A third of the files analyzed were incomplete because of a lack of information. The possible reasons for this missing data are numerous and probably

interrelated. First, it may be wondered whether the numerous items very specific to VTE were perhaps poorly understood. But there is definitely another explanation for the incompleteness of the information sheets and it may be inherent to the layout of the sheet itself. Many items such as the patient's age, past medical history and kidney function were absent from the original MDT sheet initially used. To improve data collection, a new sheet was developed based on the data that was inaccurate or missing from the original sheet (Appendix). Of course, videoconferencing during the MDT meetings makes it possible to collect any information initially missing from the sheets.

## CONCLUSION

The setting up of thrombosis MDT meetings in a university hospital fulfills a medical need in the management of VTE, with the requests for meetings ever increasing. These requests relate not only to cancer-related VTE but also to provoked and unprovoked VTE. The setting up of MDT meetings leads to changes in patient management, although the long-term impact of decisions arising from these meetings remains to be investigated.

## CONFLICTS OF INTEREST

The authors state that they have no conflicts of interest to declare.

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Figure 1 title: Patients analysed in the multidisciplinary team meetings.

Figure 1 legend: VTE means venous thromboembolism. Unspecified VTE corresponds to VTE without information about the etiology.

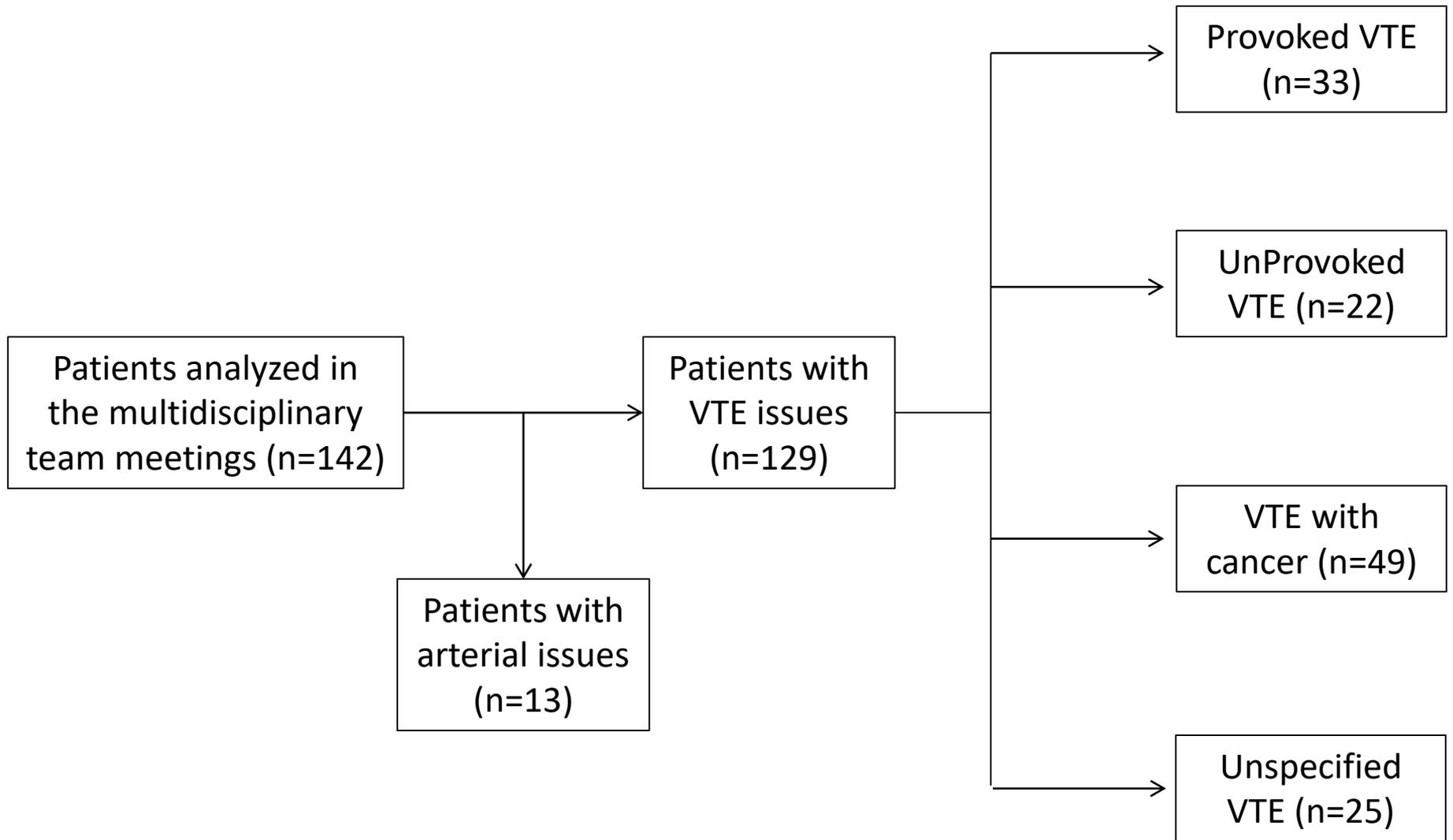


Table 1: Characteristics of the population studied in multidisciplinary team meetings.

	Provoked VTE (n=33)	Unprovoked VTE (n=22)	Cancer (n=49)	Unspecified VTE (n=25)
Mean age (years)	47+/-18	53+/-19	53+/-19	53+/-19
Men/Women	12/21	11/11	16/33	15/10
Personal VTE history (Yes/No/ND)	9/18/16	4/17/1	1/47/1	4/13/8
Family VTE history (Yes/No/ND)	6/3/24	4/5/13	2/0/47	2/10/13

VTE: venous thromboembolism; ND: no data. Unspecified VTE corresponds to VTE without information about the etiology

Table 2 Therapeutic decision about the anticoagulation

	Before multidisciplinary team meeting				After multidisciplinary team meeting				p value
	Type of anticoagulation				Type of anticoagulation				
	None	Curative	Prophylactic	Stop	None	Curative	Prophylactic	Stop	
Provoked VTE (n=33)	9	22	2	0	6	13	7	7	<0.05
Unprovoked VTE (n=22)	3	18	1	0	1	12	3	6	<0.05
Cancer(n=49)	6	40	3	0	0	40	4	5	<0.05
Total	18	80	6	0	7	65	14	18	<0.05

Legend : VTE means venous thrombo-embolism.

Table 3 title : Therapeutic decision about the choice of anticoagulants

	Before multidisciplinary team meeting				After multidisciplinary team meeting				p value
	Type of anticoagulation				Type of anticoagulation				
	Heparin	VKA	DOA	NS	Heparin	VKA	DOA	NS	
Provoked VTE	10	5	9	0	5	4	11	0	0.49
Unprovoked VTE	4	4	8	3	2	1	10	3	0.58
Cancer	36	3	1	3	33	4	7	0	<0.05
Total	50	12	18	6	40	9	28	3	0.21

Table 3 legend : VKA : Vitamin K agonist, DOA: Direct oral anticoagulant, NS: not specified. Please note that:i) for provoked VTE, 9 patients did not receive any treatment before the meeting; ii) for unprovoked VTE, 3 patients did not receive any treatment before the meeting; and iii) for cancer, 6 did not receive any treatment before the meeting. After the meeting, anticoagulants were stopped for some patients.

Table 4 title : Duration of anticoagulation

	Before multidisciplinary team meeting			After multidisciplinary team meeting			p value
	Duration of anticoagulation			Duration of anticoagulation			
	Short	Extended	ND	Short	Extended	ND	
Provoked VTE	2	4	27	7	13	6	<0.05
Unprovoked VTE	0	5	14	0	10	6	<0.05
Cancer	2	14	27	7	32	5	<0.05
Total	4	23	68	14	55	17	<0.05

Table 4 legend : VTE means venous thromboembolism. ND means no data. Please note that after the meeting, anticoagulants were stopped for some patients and was resumed for other patients.