

Outcomes after DVT: resolution, recurrence, reflux & PTS

Michelle Bonfield
University Hospitals Bristol

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Rationale for my research

The three questions most commonly asked by patients with a DVT are:

1. When will it go away?
2. Will I get it again?
3. Will it do any permanent damage?



Not every patient that has a DVT will develop a recurrent DVT or PTS but there is a lack of research evidence to indicate which patients will, making these difficult questions to answer.

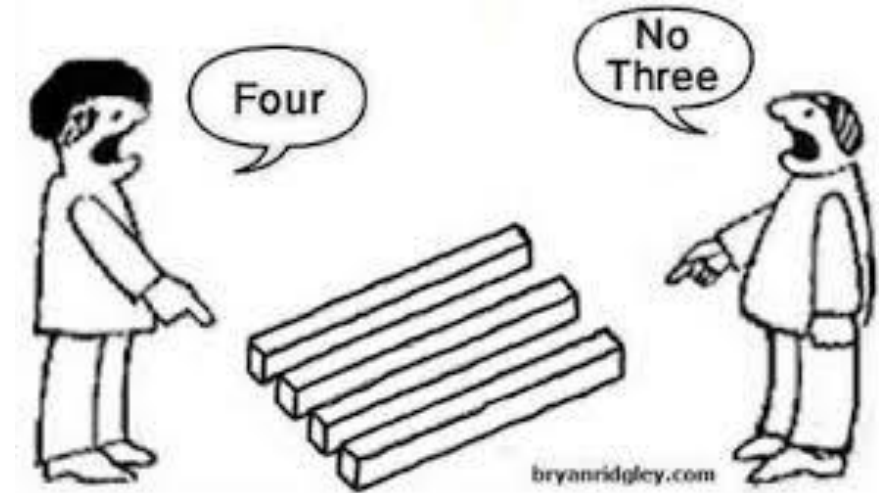
Why is it important?

- Patients with PTS worse QoL scores than average scores for diabetes, chronic lung disease and osteoarthritis (Kahn *et al*, 2008).
- Total health care cost per DVT patient almost 50% greater in those with PTS than those without over 2 years post diagnosis (Guanella *et al*, 2011).
- Debate whether prolonged anticoagulation could benefit certain patient groups.
- Endovenous intervention - invasive, expensive & requires careful risk stratification, works best in acute stage but early identification remains challenging.

Preparation for the study



Peer group opinion



Systematic literature review

Limitations of previous studies



- Poorly described methods
- Selection bias
- Detection bias
- Attrition bias
- Blinding

Methodological



- People can come up with statistics to prove anything, Kent. Forty percent of people know that.

Statistical Analysis



- “Complications” post DVT likely to be correlated with each other
- Confounding was a major issue: if no regression analysis, cannot be sure variables are independent of each other.

Small sample sizes



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Peer Group Opinion

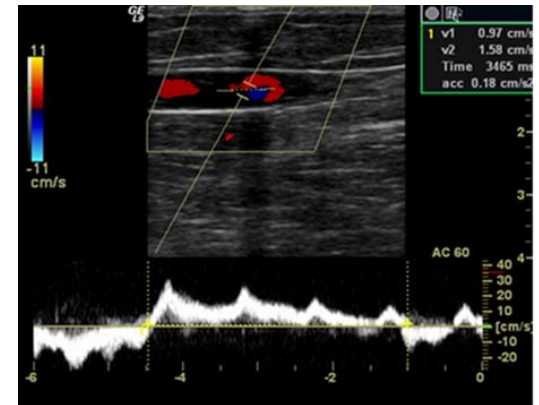
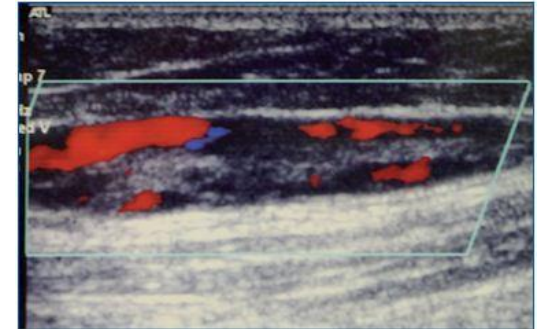


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Potentially important factors in the development of PTS	Category with the largest % of the respondents	%
Extent of original DVT	Related & very important	73
Combination of residual obstruction and reflux	Related & very important	71
Previous ipsilateral DVT	Related & very important	67
Presence of deep venous reflux	Related & very important	67
Residual thrombus	Related & very important	56
Iliac involvement of original DVT	Related & very important	42
Insufficient quality of anticoagulation	Related & very important	40
Poor compliance with compression hosiery	Related	52
Reflux duration	Related	50
BMI	Related	48
Location of original DVT	Related	46
Calf muscle pump function	Related	44
Transient versus permanent risk factors	Related	38
Pre-existing superficial venous reflux	Related	33
Thrombophilic status	Related	33
Peak reflux velocity	Related	31
Malignancy	Related	29
Bilateral DVT at presentation	Related	27

Observational Study

- Using ultrasound imaging to examine :
 - Changes in thrombus load over time
 - How quickly the DVT resolves
 - Resolution extent by end of treatment
 - Any extension to original DVT
 - Any recurrence during follow up period
 - Development of venous reflux
- Patients with first episode of DVT
- 6 visits over 2 years: 1 week, 1 month, 3 months, 6 months, 1 year, 2 years



Thrombus Load Score

Study ID and Venous Segment	Follow-up interval						
	0 days	7 days	1 month	3 months	6 months	12 months	24 months
PTS0926							
Inferior Vena Cava	0	0	0	0	0	0	0
Common Iliac Vein	0	0	0	0	0	0	0
External Iliac Vein	0	0	0	0	0	0	0
Common Femoral Vein	0	0	0	0	0	0	0
Profunda Vein	0	0	0	0	0	0	0
Proximal Femoral Vein	3	3	3	1	1	1	0
Distal Femoral Vein	3	3	3	3	3	3	1
Popliteal Vein	3	3	3	3	3	3	3
Peroneal Veins	3	3	2	0	0	0	0
Posterior Tibial Veins	3	3	2	0	0	0	0
Anterior Tibial Veins	0	0	0	0	0	0	0
Soleal Veins	2	2	0	0	0	0	0
Gastrocnemius Veins	2	2	0	0	0	0	0
Greater Saphenous Vein	0	0	0	0	0	0	0
Short Saphenous Vein	0	0	0	0	0	0	0
Total	19	19	13	7	7	7	4

Fifteen venous segments assigned a thrombus score at each visit:

0 = patent

1 = sub-segmental, non-occlusive

2 = sub-segmental, occlusive

3 = occlusive thrombus throughout

Data Analysis

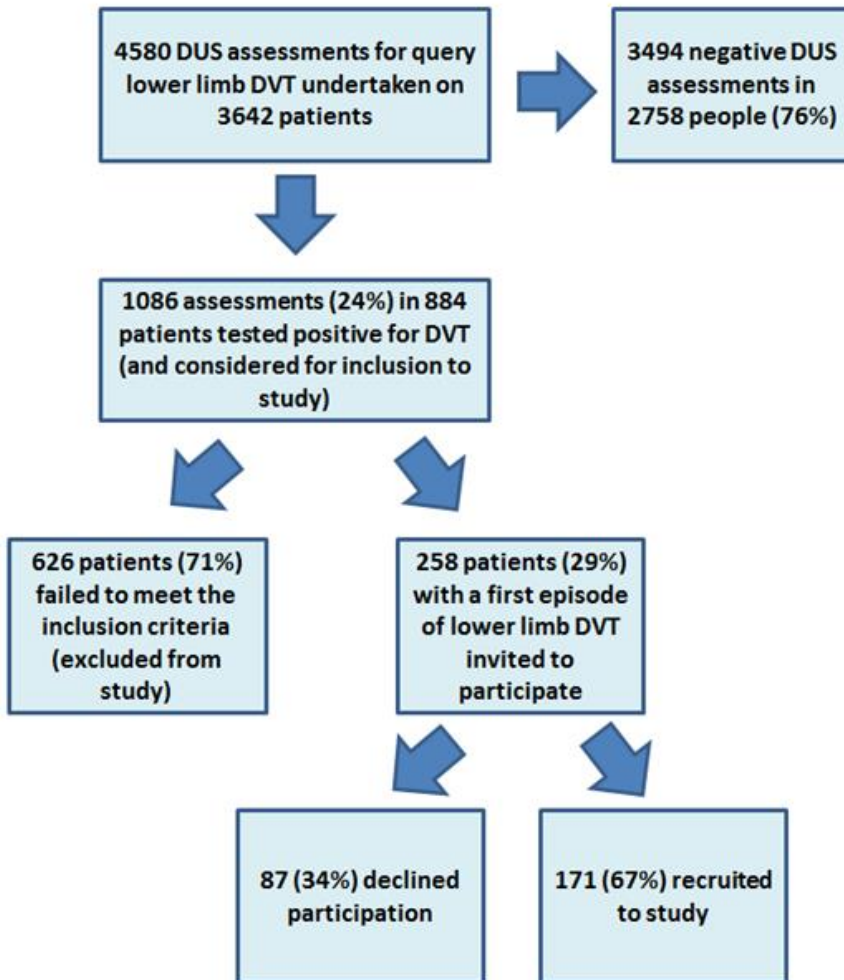


- Logistic regression – identify relationships between baseline characteristics/those presenting during follow-up and primary endpoints

- **Primary endpoints**
 - DVT resolution
 - Recurrence
 - New reflux
 - Development of PTS



Recruitment



Reason for exclusion	n	%
Immobility	171	27.3
Intravenous drug user (IVDU)	157	25.1
Active Cancer	147	23.5
Previous ipsilateral DVT	63	10.0
Non acute DVT	47	7.5
Unable to give informed consent	24	3.8
Her Majesty's Prison (HMP)	8	1.3
Pregnant	6	1.0
Risk to lone worker	3	0.5
Total	626	100.0

DEMOGRAPHICS

	All scans n (%)	All +ve scans n (%)	Declined n (%)	Recruited n (%)
Total number of patients	3642	884	87	171
Mean age	60.9 ±19.7	58.6 ±18.8	60.0 ±17.4	55.9 ±16.5
Age range	15 - 101	20-97	22-90	21-85
Men	1559 (43)	488 (55)	44 (51)	105 (61)
Women	2083 (57)	396 (45)	43 (49)	66 (39)
Outpatients	2773 (76)	670 (76)	87 (100)	171 (100)
Inpatients	869 (24)	214 (24)	0 (0)	0 (0)
Bilateral assessments	397 (9)	39 (6)	0 (0)	3 (2)
Multiple visits	427 (12)	127 (14)	N/A	N/A
2 visits	351	103	N/A	N/A
3 visits	52	19	N/A	N/A
4 visits	15	3	N/A	N/A
5 visits	7	1	N/A	N/A
6 visits	1	1	N/A	N/A
7 visits	1	0	N/A	N/A

Retention



Complete Data Sets (n = 171 participants)	n	%
1 week	171	100
1 month	165	97
3 months	163	95
6 months	160	94
1 year	156	92
2 years	147	86

5 deceased:
3 Cardio-vascular
2 Cancer

19 withdrew:
10 lost to follow-up
6 no time
1 too unwell
2 mental health



Participants



90 Male and **57** female

Age range **21-85** years (mean 57 years +/- 16 years)

90 Left Leg, **98** Provoked

9 ileo-fem, **67** femoral, **71** distal

27 concurrent phlebitis, **7** previous contralateral DVT

3 underweight, **32** normal weight, **112** overweight

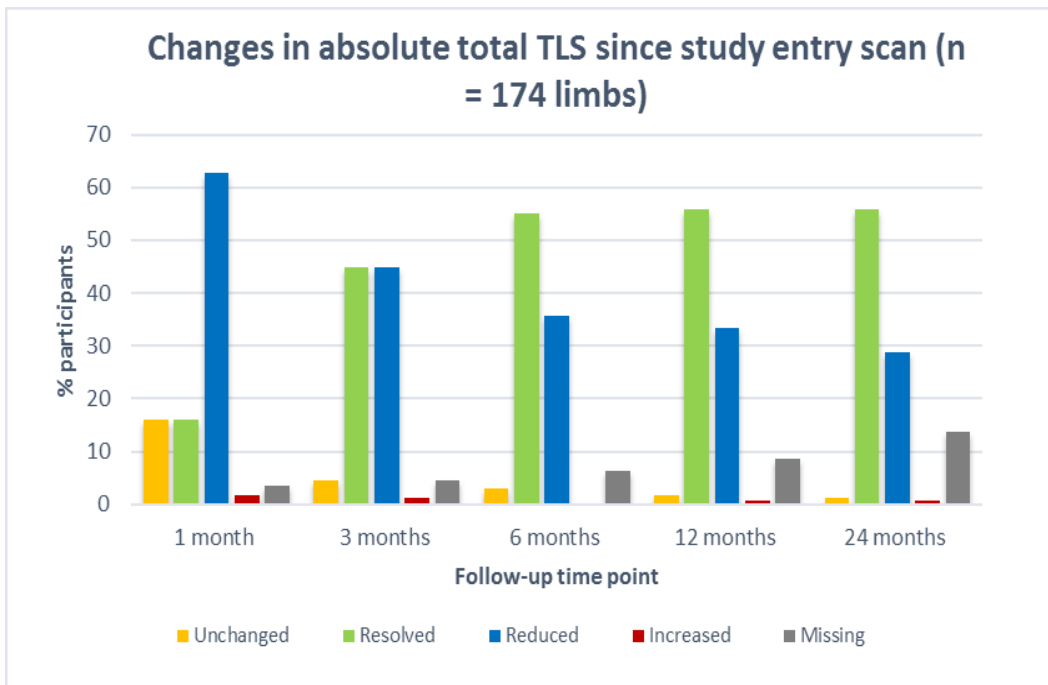
23 current smokers, **53** ex-smokers, **71** never smoked

11 Diabetes, **39** Hypertension, **1** Heart Failure

128 DOACs, **18** LMWH & warfarin, **1** aspirin only



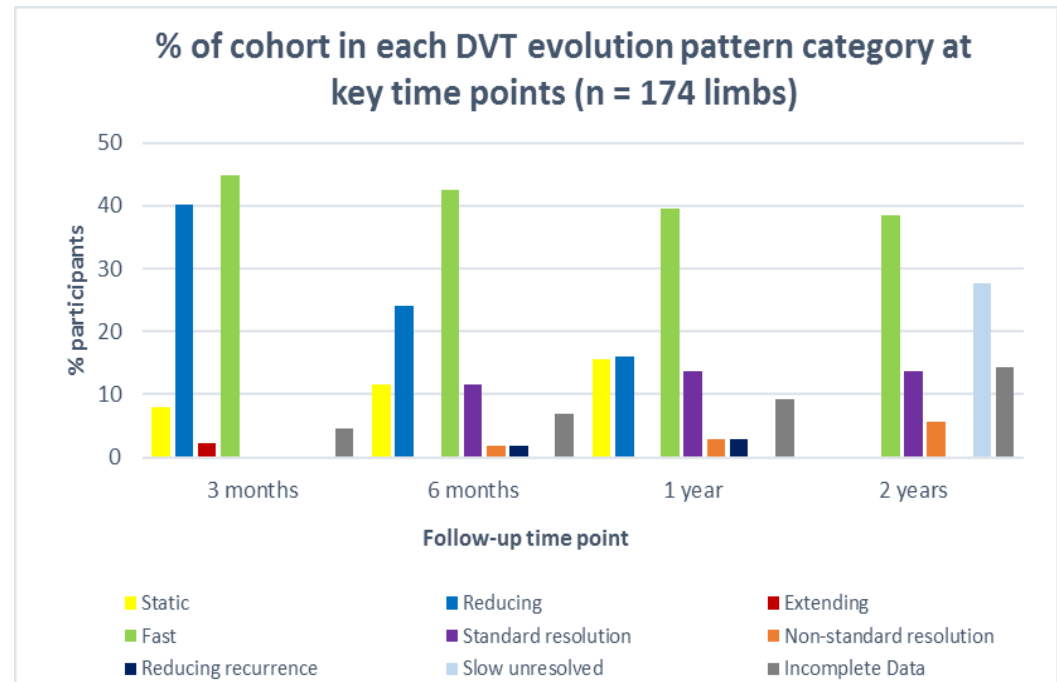
Changes in thrombus load



Grading	Definition
Unchanged	No change in TLS compared to TLS at ref point
Zero	TLS = 0
Reduced	Reduction in TLS compared to TLS at ref point
Increased	Increase in TLS compared to TLS at ref point

Thrombus Evolution Patterns

DVT Evolution Category	Definition
Static	No change in thrombus burden
Reducing	Continued decrease at each follow-up visit up to one year
Extending	Increase in thrombus burden during first three months
Fast resolution	Resolution* within three months
Standard resolution	Continued decrease at each follow-up visit with resolution within one year
Non-standard resolution	Not following standard resolution pattern but resolved by two years
Reducing recurrence	Recurrence of DVT after initial resolution but followed by subsequent ongoing resolution
Slow unresolved	Some reduction in thrombus burden over two years but incomplete resolution

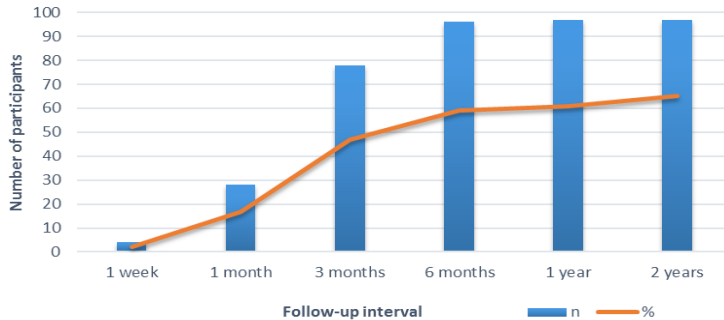


Thrombus Evolution Patterns

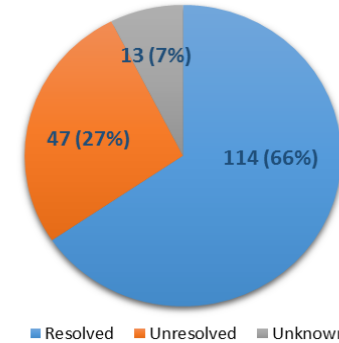
Evolution pattern at 3 months post DVT	Evolution pattern at 2 years post DVT	Number of cases
Static (n=14)	Non-standard resolution	6
	Slow unresolved	7
	Missing	1
Reducing (n=70)	Standard resolution	22
	Non-standard resolution	3
	Slow unresolved	40
	Missing	5
Extending (n=4)	Standard resolution	2
	Non-standard resolution	1
	Slow unresolved	1
Fast (n=78)	Fast	67
	Missing	11
Missing (n=8)	Missing	8

DVT Resolution

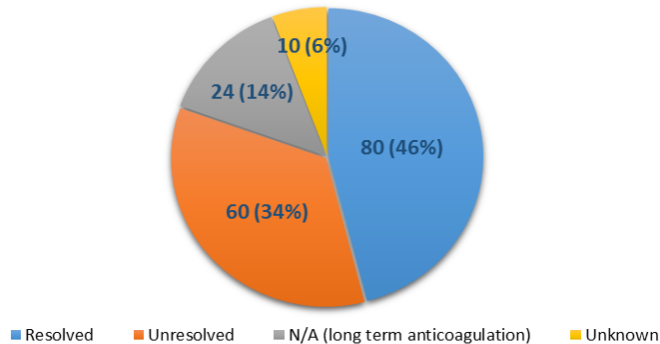
DVT resolutions at each follow-up time point
(1st episode DVT Group, n = 174)



Resolution of index DVT within 24 months (n = 174 limbs)



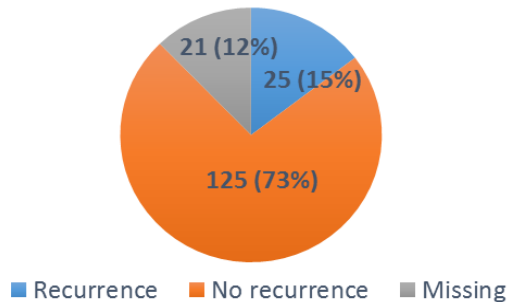
Resolution of index DVT at point of stopping
anticoagulation therapy (n = 174 limbs)



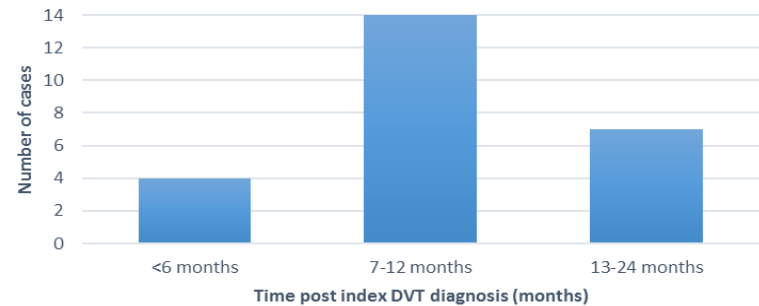
- Almost half no significant change in first 7 days
- Majority had reduction in thrombus in first month
- Large increase in resolutions between 1-3 months
- Initial period of significant change first 3 months
- Only approx. half resolved by end of treatment
- About third remained unresolved at 2 years

DVT Recurrence

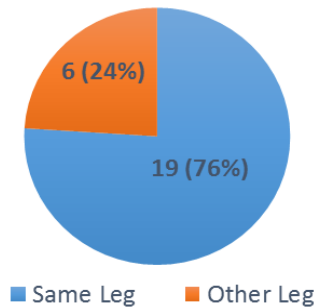
DVT recurrence during 24 months post index DVT diagnosis (n = 171 participants)



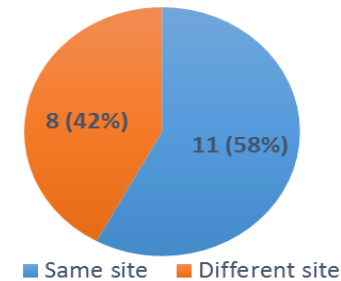
Time of DVT recurrence in months in relation to the index DVT diagnosis date (n = 25 participants with DVT recurrence)



Distribution of DVT recurrences in relation to index DVT (n = 25 participants with DVT recurrence)

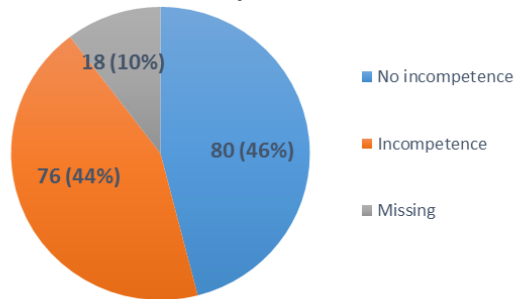


Distribution of ipsilateral DVT recurrences in relation to index DVT (n = 19 participants with ipsilateral recurrence)

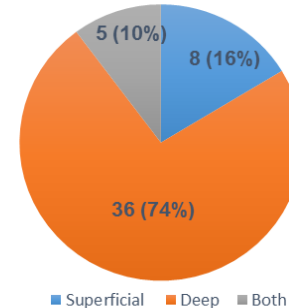


Venous Incompetence

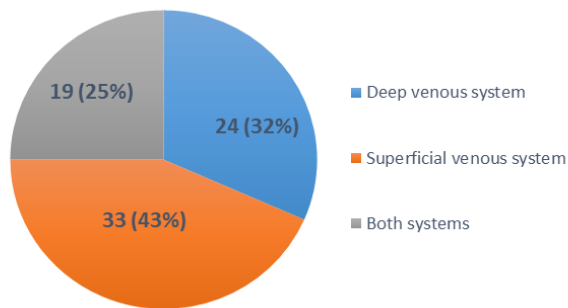
Detection of venous incompetence in any vein during 24 month follow-up (n = 174 limbs)



Location of newly developed venous incompetence within 24 months of index DVT diagnosis (n = 49 limbs)

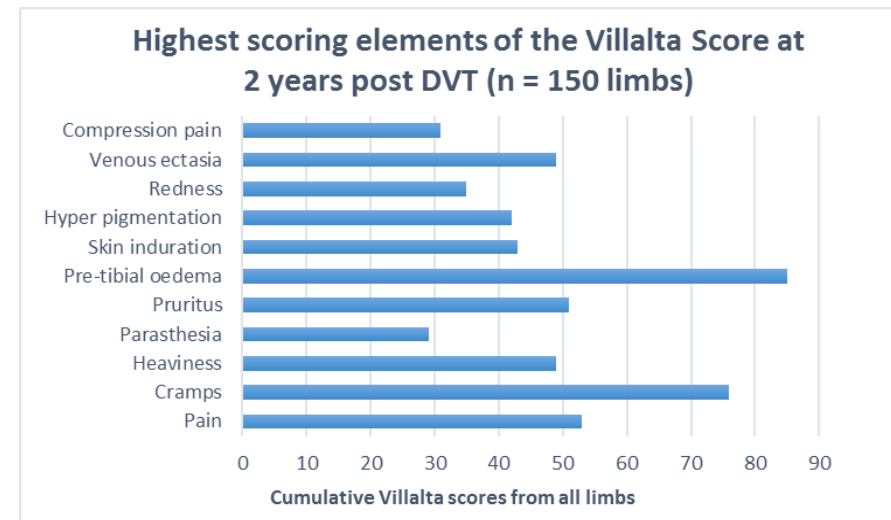
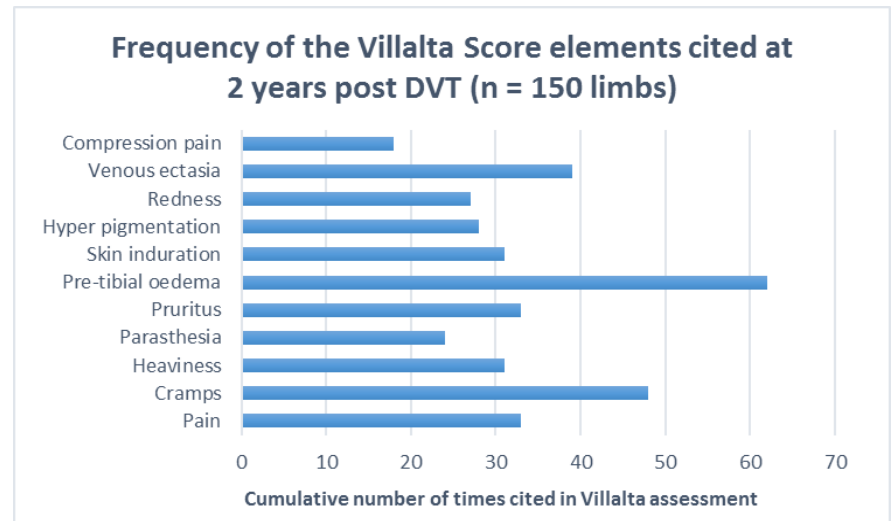
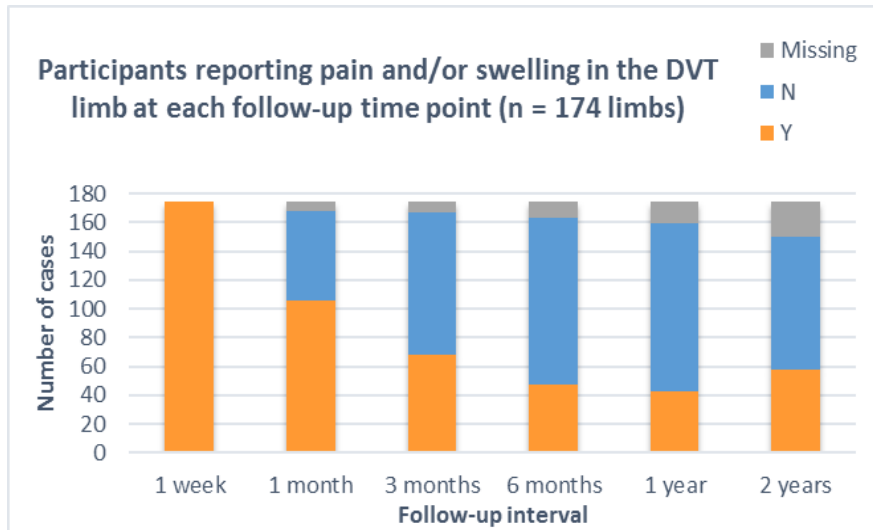


Distribution of venous incompetence (n = 174 limbs)



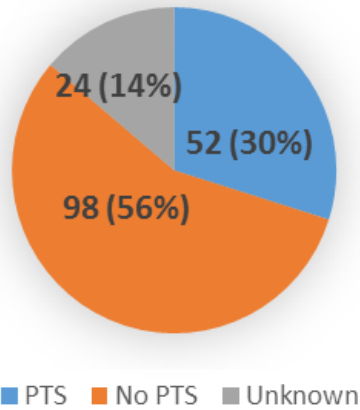
- New reflux developed in 28%.
- Majority new reflux occurred in deep venous system.
- Pre-existing superficial reflux detected in third of limbs that later developed reflux in deep veins during 2 year follow-up.

Development of PTS

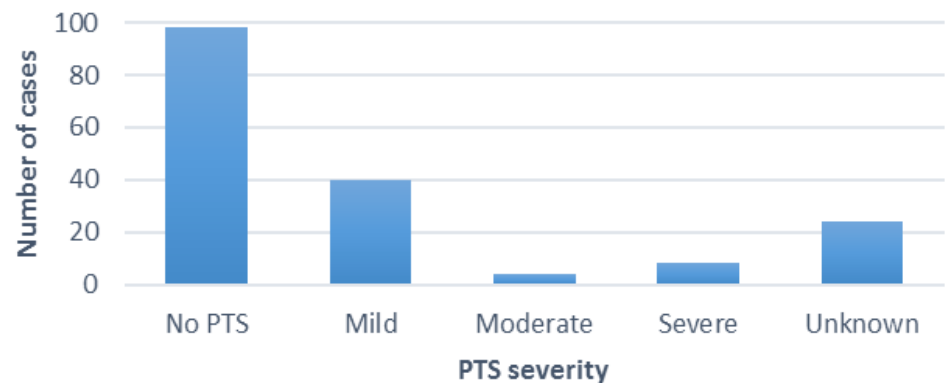


Development of PTS

Development of PTS at 2 years (n = 174 limbs)



PTS cases and severity (n = 174 limbs)



Examining Associations

1. Cross tabulation:

DVT location & index DVT resolution within & index DVT resolution within 24 months			
Missing predictor variable = 0, Missing outcome variable = 13			
DVT location	Index DVT resolved n (%)	Index DVT not resolved n (%)	Total n (%)
Distal	79 (96)	3 (4)	82 (100)
Proximal	32 (42)	44 (58)	76 (100)
Total	111 (70)	47 (30)	158 (100)

(OR =36.2;95% CI 10.5 – 125.1, p<0.001))

= unadjusted odds ratio

2. Chi Squared = confirm potentially significant variables $P < 0.05$

3. Logistic regression = adjusted odds ratios (confounding factors)



Relationships

Dependent Variable	Resolution	Recurrence	Incompetence	PTS
Age	X	✓	X	X
Gender	X	X	X	✓
BMI	X	X	X	✓
Treatment type	X	✓	✓	X
Treatment duration	X	X	X	X
Smoking history	X	X	X	X
Hypertension	X		X	X
TLS at diagnosis	✓	X	X	X
DVT location	✓	X	✓	X
Provocation status	X	X	X	X
Pre-existing venous incompetence	X	X	X	
Stocking use	X	X	✓	✓
Concurrent phlebitis at DVT diagnosis	X	X	X	X
Duration of symptoms before treatment	X	X	X	X
Index DVT resolved within 24 months		X	X	✓
Thrombus evolution pattern at 3 months			X	X
DVT recurrence			X	X
New phlebitis during follow-up			X	X
Venous incompetence				✓

Strength of Relationships

- Distal DVT & lower thrombus burden much more likely to resolve

OR = 16.7 (95% CI 4.55 – 61.1, $p = <0.001$)

OR = 9.95 (95% CI 3.02 – 32.7, $p = <0.001$)

- Reflux more than twice as likely with proximal DVT

OR = 2.58 (95% CI 1.13 – 7.63, $p = <0.05$)

- Rivaroxaban – lower reflux & recurrence rates.

OR = 4.85 (95% CI 1.46 – 16.1, $p = <0.05$) (LMWH & warfarin)

OR = 3.16 (95% CI 1.06 – 9.46, $p = <0.05$) (LMWH & warfarin)

Strength of Relationships

- PTS associated with:

Female **OR = 2.29** (95% CI 1.01 – 5.21, $p = <0.05$)

Overweight **OR = 4.54** (95% CI 1.43 – 14.40, $p = <0.05$)

Residual clot, **OR = 3.02** (95% CI 1.20 – 7.57, $p = <0.05$)

No stockings **OR = 2.65** (95% CI 1.11 – 6.31, $p = <0.05$)

Superficial reflux **OR = 4.27** (95% CI 1.44 – 12.69, $p = <0.01$)

Implications of study findings

- Better prepare patients for outcomes after DVT - manage expectations or anxiety.
- Positive longer term outcomes after Rivaroxaban use.
- Risk stratification for PTS.
- Lifestyle advice – weight management, stocking use.
- DOACs safe for overweight patients?
- Incompetence – valve damage from DVT may not be the reason.
- Extended anticoagulation may not be beneficial.

Limitations



- Selected population
- Establishing baseline
- Subjectivity Villalta scale
- Loss to follow up
- 2 years follow-up

Strengths



- Topical
- New info re DOACs
- Good sample size
- Published protocol
- Data quality

Future Research

- Larger study, longer follow-up, targeting specific questions
- Prediction model and clinical risk scoring tool for PTS
- Psychological impact of DVT

Thank you for listening