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Upper Extremity Deep Venous Thrombosis (UEDVT)

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Abstract

Upper extremity Deep Venous Thrombosis (UEDVT) is frequent in the hospital, especially in the intensive care unit. It often complicates the placement of central venous catheters (CVC), notably peripherally inserted central (PICC) lines. Despite a lower rate of pulmonary embolism, UEDVT is as fatal as lower extremity DVT. This is due to its strong association with cancer. Symptoms are often absent, but systematic screening is not recommended. The best prophylaxis is good central catheter management. Pharmacological prophylaxis has questionable effectiveness in the prophylaxis of CVC-associated UEDVT. Compression ultrasonography is the first line diagnostic tool. Treatment is anticoagulation for at least 3 months. A causative central line should be removed as soon as clinically possible. Infrequently, patients with the thoracic outlet syndrome can get an effort related primary UEDVT. It is also known as the Paget-Schroetter syndrome. Along with anticoagulation, surgical referral for decompression of the thoracic outlet is then necessary. The current state of evidence on UEDVT is rather poor, due to the absence of large randomized controlled trials.

Keywords: Venous thromboembolism; Deep venous thrombosis; Upper extremity; Central venous catheter thrombosis

Case Presentations

Case 1

The nurse from the medical-surgical unit calls the attending physician because she is unable to flush the right arm peripherally inserted central (PICC) line of a 60-year-old female getting intravenous vancomycin. The nurse wonders whether a new PICC line needs to be placed to complete the 5 remaining days of the antibiotic course.

Case 2

A 22-year-old left-handed college student developed left arm swelling while painting her apartment. Overnight, the arm started swelling and the worsening pain brought her to the ER. She is otherwise healthy; her only medication is oral contraceptives.

Introduction

The veins of the upper extremity: deep and superficial

The veins of the upper extremity are responsible for 5% to 10% of the cases of venous thromboembolism (VTE) [1]. A superficial venous thrombosis is the formation of a thrombus in the superficial venous system that includes the cephalic and basilic veins. It is often self-limited. A deep venous thrombosis (DVT) is the formation of a thrombus in the deep venous system, mainly in the brachial, axillary and subclavian veins. It can be lethal. An UEDVT can extend to the brachiocephalic veins and to the superior vena cava, it can embolize to the lungs, and it can lead to long-term disability related to the post-thrombotic syndrome (PTS).

The thoracic outlet is the space confined between the clavicle and the first rib. It can be the site of the compression of various neurologic and vascular structures including the subclavian vein. The clinical manifestations of such compression are grouped under the thoracic outlet syndrome. One of these manifestations is the venous thrombosis of the subclavian vein, usually preceded with repetitive effort of the upper extremity; it is therefore named 'effort related UEDVT' or the 'Paget-Schroetter syndrome'. Internal jugular venous thrombosis is often included in the studies addressing the UEDVT, despite its anatomical location in the neck.

UEDVT classification: Primary vs. Secondary

Primary	Secondary
Minority	Vast majority
Mainly caused by the Paget-Schroetter syndrome. Less likely idiopathic	Caused by central venous catheters, pacemaker leads or cancer
Younger patients	Older patients

Table 1: UEDVT classification.

As shown in Table 1, most cases of UEDVT are secondary. Patients with idiopathic primary UEDVT, when compared to effort related primary UEDVT i.e., the Paget-Schroetter syndrome, tend to be older with a female predominance [2].

High and increasing incidence of UEDVT

UEDVT is infrequent in the general population. Its incidence however increases exponentially when moving to the hospital setting,

mainly the intensive care unit (ICU) (Table 2). The incidence of UEDVT is on the rise and parallels the increase in PICC line use.

Setting	Yearly Incidence	Study
Population, Malmö, Sweden	0.0036%	Isma, N., et al. (2010). (3),
Population, Worcester, MA	0.016%	Spencer, F. A., et al. (2007). (4)
Medical inpatients admissions	0.14%	Winters, J. P., et al. (2015)(5).
Hospital discharges	1.15%	Khanna, R., et al. (2014)(6)
ICU, secondary and tertiary	2.2%	Lamontagne, F., et al. (2014)(7)

Table 2: Incidence of UEDVT.

UEDVT vs. Lower extremity DVT (LEDVT): same mortality

Despite a lower rate of pulmonary embolism (PE) on presentation, patients with UEDVT compared to LEDVT had similar mortality outcomes in the RIETE registry [8] and in the review of the medical records of all the residents of Worcester, MA [4]. Smaller studies showed even worse mortality outcomes with UEDVT(9), and estimated the UEDVT mortality rate as 5.4 times (4.2 to 7 CI 95%) higher than the age and sex adjusted population mortality rate [10].

Note that patients with UEDVT tend to be younger and slimmer than LEDVT patients [11,12].

Critical appraisal of the literature

Pubmed.gov was researched for articles published before October 15, 2015, using the keywords "deep venous thrombosis or it's abbreviation 'DVT' or venous thromboembolism or it's abbreviation 'VTE' or thrombophlebitis AND upper extremity" as well as "central line thrombosis" and "central venous catheter or it's abbreviation 'CVC' thrombosis". Filters that were used: articles in English, full text available and humans.

Most articles unique to the pediatric population were later removed unless the data could be extrapolated to the adult cases. Clinicaltrials.gov was researched for ongoing trials. The Agency for Healthcare Research and Quality (AHRQ) and the Joint commission websites were used for info about the Patient Safety Indicator (PSI) #12 and the VTE core measure.

The review of the literature points toward many small prospective and retrospective studies addressing the risk factors for UEDVT. Major randomized controlled trials addressing the therapy and prophylaxis of UEDVT are lacking. Guidelines are often extrapolated from trials done on LEDVT. The 2012 American College of Chest Physicians (ACCP) guidelines [1] rate the current quality of evidence as being 'at best, moderate'.

Etiology and Pathophysiology

Central venous catheters (CVC) notably PICC lines and malignancy are the main causes of secondary UEDVT. The thoracic outlet syndrome is the main cause of primary UEDVT.

Central venous catheters and pacemaker leads

CVC (subclavian, internal jugular, PICC lines, Hickman catheters etc.) or pacemaker leads placement is the strongest independent predictor of UEDVT. UEDVT cases were, in a case-control study, 1136 times more likely to have a CVC compared with control subjects with no UEDVT [13]. Patients with a CVC were, in a prospective registry, 7.3 (CI 5.9 to 9.2, 95%) times more likely to get an UEDVT than non-CVC patients [12]. The percentage of UEDVT that is associated with a CVC or pacemaker leads varies between studies but is usually higher than 50% (appendix 1).

The incidence of CVC thrombosis varies greatly between studies. It tends to be higher whenever systematic imaging is performed. Thirty-three percent of screened catheters in an ICU [14] and 56% of screened cardiac surgery patients [15] had an UEDVT. Numbers are more modest (below 10%) when only symptomatic cases are accounted for [16,17].

The infusion of veno-toxic substances like chemotherapy and vancomycin [18] tends to cause more UEDVT compared to the infusion of veno-toxic ones like parenteral nutrition.

PICC lines

The risk of UEDVT associated with PICC line insertions is high and worse than non-peripherally inserted central lines [19,20]. UEDVT is responsible for the removal of 2 to 3% of placed PICC lines [21,22]. The incidence of PICC associated UEDVT varies drastically between studies (<1% to >70%; appendix 2). The number of PICC lines that are placed is so high, that even in studies with low incidence of PICC line associated UEDVT, a significant portion of all UEDVT is still due to PICC lines: in Liem, T.K, et al. 35% of all UEDVT were caused by PICC lines, despite a low incidence of 2.6% [23].

Subcutaneously implanted port-chamber catheters

Cause less thrombosis than PICC lines with no significant increased cost, as shown in a prospective study of 70 patients undergoing chemotherapy for non-hematological malignancies [24]. The incidence of UEDVT is in the single digit (around 2%) in most studies (appendix 3).

Hickman Catheters

A retrospective study comparing PICC lines to Hickman catheters in acute myeloid leukemia showed a much better thrombotic profile with the Hickman catheter: 48.2% with PICC lines versus 3.2% with Hickman catheters [25]. Higher thrombosis rate (17%, some upon autopsy) was found in a study of 168 patients with solid tumors, particularly patients with lung adenocarcinoma [26].

Pacemaker leads

Pacemaker leads Venography, in a prospective study, was abnormal in 64% of the 202 patients. Patients with low ejection fraction or a previous temporary pacemaker were identified as risk factors [27].

Malignancy

Malignancy was the only independent predictor of the incidence of non-leg deep venous thrombosis in a prospective cohort of 3746 ICU patients [7]. Occult malignancy was found in 23.7% of cases of UEDVT compared with 11.1% of the cases of LEDVT in a study of 343

consecutive patients with DVT [28]. The mortality of patients with UEDVT is high, mainly because of its association with cancer. In the Malmö thrombophilia study, 24% of the patients with UEDVT died during Follow up and mortality was as high as 47% in patients with known malignancy [3]. Cancer patients with UEDVT in the RIETE registry had worse outcomes [8].

Other risk factors

Aside from CVC and malignancy, there are other risk factors for UEDVT: chronic kidney disease [29,30], hormone therapy [3], obesity [13] and infection or sepsis [31-33]. The relation between CVC thrombosis and infection goes both ways since a thrombosed CVC is a risk factor for CVC related sepsis [14].

Hereditary thrombophilia has less impact in UEDVT compared to LEDVT [11,34,35], especially in CVC-induced UEDVT(36). The rate of thrombophilia in UEDVT has been addressed in small studies. It ranges between 6 to 9% [37] to 42% in a series of cases of primary UEDVT [2].

Special risk factor: the thoracic outlet syndrome in the Paget-Schroetter syndrome

MRI imaging of the costoclavicular distance was significantly narrower in patients with primary UEDVT when compared to normal cases [38]. Patients with the thoracic outlet syndrome undergoing first rib resection when compared to cadaveric first ribs, were found to have a bony tubercle at the site of the subclavian vein groove causing extrinsic compression of the subclavian vein at rest [39].

Initial Evaluation (Table 3)

History & physical examination: suspected acute UEDVT

Symptoms are frequently absent. The rate of asymptomatic patients varies widely between studies (12% to 94%) [40-42]. In the absence of symptoms, an UEDVT is diagnosed when a CVC is not functioning appropriately or when imaging is performed for a different reason.

Pain and edema are the predominant clinical symptom and sign of UEDVT. In a series of mostly CVC-associated UEDVT, pain and edema were present in 34% and 84% of the cases respectively [43]. Severe syndromes including the superior vena syndrome and the phlegmasia dolens of the upper extremity have been reported. Thrombosis in the brachiocephalic veins and the superior vena cava was retrospectively estimated to have been diagnosed in 0.03% of the patients; the diagnosis had been preceded with symptomatic PE in more than a third of the cases [44].

The use of the Constans Clinical Prediction score (Table 4) is a simple validated score to clinically predict the risk of a suspected UEDVT.

History	Physical examination
Pain	Edema, erythema or discoloration of the skin
Presence of CVC, port or pacemaker	Dysfunction of the CVC, port or pacemaker
Hormone therapy, malignancy, history of thrombophilic states or previous venous thrombotic event.	Signs of PE: tachycardia, tachypnea, hypoxia.
Effort (repetitive like painting, volleyball hitter etc) in primary UEDVT	

Table 3: Elements to consider upon the initial evaluation of (a suspected) UEDVT.

Item	Point
Catheter or access device in a subclavian or jugular vein or a pacemaker	+1
Unilateral pitting edema	+1
Localized pain	+1
Other diagnosis at least as plausible	-1
Total Score	**Prevalence of UEDVT**
-1 or 0	Low (9 to 13%)
1	Intermediate (20 to 38%)
2 or 3	High (64 to 70%)

Table 4: The Constans Clinical Prediction Score [45].

History & physical examination: suspected post-thrombotic syndrome (PTS)

The PTS, a long-term complication of DVT, is due to symptomatic venous insufficiency. It is thought to occur in around 20% of the patients [1] but the incidence varies considerably between studies (6% to 44%) [9,46,47]. The severity of the syndrome is often assessed with the Villalta scoring system that has been validated for the lower extremity [48] (Table 5).

Symptoms	Signs
Pain	Edema
Cramps	Skin induration
Heaviness	Hyperpigmentation
Paresthesias	Redness
Pruritus	Venous ectasia
	Pain on calf compression
	Venous ulcer implies severe PTS

Table 5: Symptoms and signs of the post-thrombotic syndrome as in the Villalta scoring system.

Patients with idiopathic UEDVT tend to be young. The PTS can severely affect their quality of life. Data however shows that the overall quality of life after treatment is satisfactory [49].

Diagnostic Studies

Data is extremely limited. The extrapolation from LEDVT studies is challenging given the different anatomy of the UE where a portion of the deep venous system runs under the clavicle.

Duplex ultrasound

Contrast venography is the gold standard diagnostic test. It is not recommended as a first line diagnostic study given the need for intravenous contrast. Compression ultrasonography is indeed the first line diagnostic study, with a sensitivity and specificity estimated at 97% and 96% respectively in a systematic review of 9 studies [50]. The sensitivity and specificity did interestingly not improve with the addition of Doppler. The risk of false negative ultrasound increases in the proximal subclavian [51] given its anatomical location.

Ddimer in a series of 52 consecutive patients, of whom 23 had cancer, had a sensitivity of 100% (95% CI, 78–100%) and a specificity of 14% (95% CI, 4–29%) [52]. The lab might therefore be valuable to the screening of unlikely UEDVT, similar to its usage in the diagnosis of LEDVT.

Others imaging modality

A chest X-ray is an appropriate first test when suspecting the thoracic outlet syndrome. It is a cheap and a safe modality to detect bone abnormalities [53]. Magnetic Resonance (MR) venography is difficult for the patients [54], yet appropriate for the diagnosis of the thoracic outlet syndrome [53]. Computerized Tomography (CT) venography and contrast venography are occasionally used too.

Diagnostic algorithm

A recently published prospective multicenter study [55] showed that an algorithm combining clinical decision score (the Constans Clinical decision score Table 4), Ddimer and ultrasonography is safe and effective. If confirmed in other studies the algorithm has the potential of becoming standard of care.

The 2012 ACCP guidelines had anyway recommended, with a grade 2C, further testing using Ddimer, serial ultrasonography or venographic based imaging (traditional, CT or MR) whenever the first the clinical suspicion is high but the initial ultrasound is negative [1].

Differential Diagnosis

Superficial venous thrombosis can cause similar symptoms as UEDVT but its risk of complications including PE is very rare. The evidence behind the treatment is limited and of low quality [56]. Treatment is usually symptomatic (anti-inflammatory medications, warm compresses etc.). Unlike the superficial venous thrombosis of the lower extremity, there is no clear indication for anticoagulation. Anticoagulation might however have a role in selected cases, for example when the thrombus is extensive or close to the deep venous systems.

Non-thrombotic causes of UE edema and discoloration include the cellulitis of the UE. It also includes cases of malignant invasion or compression of the venous system by UE or chest tumors. The McCleery syndrome is a rare non-thrombotic intermittent compression of the subclavian vein causing periodic arm swelling and discoloration [57].

Prophylaxis

Non-pharmacological prophylaxis of CVC- associated UEDVT

The preferential usage of smaller gauge and single lumen PICC lines [58], the correct positioning of the tip of a CVC [59], the removal of a CVC as soon as clinically possible [60] and the usage of ultrasound for PICC line placement [61] were shown to decrease the risk of UEDVT. The laterality of a CVC is most likely not a risk factor of UEDVT [62,63], despite the presence of some contradictory evidence [59].

Pharmacological prophylaxis of CVC associated UEDVT has shown contradictory results in different studies (Appendix 4 and Appendix 5) and is therefore not recommended for routine universal usage. It might be beneficial in the subgroup of cancer patients with a CVC as shown in a Cochrane database review [64].

CVC prophylaxis with the infusion of low dose anticoagulant or with the usage of anticoagulant-coated CVC has been studied in the pediatric population with mixed results [65-71]. More data is needed.

Treatment of UEDVT (Table 6):

The removal of a thrombosed CVC

The Removal of a thrombosed CVC is not only a prophylactic measure but a therapeutic one too. It was shown to significantly decrease the clot size on ultrasound [72,73]. A CVC does however not need to be removed if the UEDVT occurs in association with a functioning and clinically needed CVC.

If the catheter is no longer required or is not functioning and cannot be made to function it should then be removed (ACCP guidelines 2012, grade 2 C) [1]. This was also shown in a small prospective study of 27 children [74].

Fibrinolytics to restore the flow of a thrombosed CVC

Different fibrinolytics including tenecteplase [75], recombinant urokinase [76,77], reteplase [78], and alteplase [79-81] were found to

be effective, safe and cost-effective in restoring the flow of a thrombosed CVC.

Anticoagulation

As previously stated, the evidence behind the effectiveness of anticoagulation is mainly inspired from LEDVT randomized controlled trials. Rare small retrospective or prospective observational studies address anticoagulation for the UEDVT [82,83].

Indication and Recommendation	Grade	Comment
Initial parenteral anticoagulation	1B	Low-molecular weight heparin or fondaparinux suggested over unfractionated heparin that is intravenous (2C) or subcutaneous (2B).
Anticoagulation alone without thrombolysis	2 C	Intensity and duration of anticoagulation unchanged if initial thrombolysis (1B)
Anticoagulation of minimum 3 months	2B	3 months sufficient if: no cancer & not CVC related (1B); CVC removed whether the patient has cancer (2C) or not (1B)
Thrombosed CVC: Not removing if functioning & needed	2C	Extend the duration of anticoagulation (beyond 3 months) until the CVC is removed, whether the patient has cancer (1C) or not (2C)
Symptomatic therapy of the PTS: sleeves, compression bandages	2C	Recommendation against the use of compression sleeves or venoactive medications for PTS prevention (2C)

Table 6: Therapy of acute UEDVT: ACCP 2012 guidelines [1].

Despite the guidelines recommending anticoagulation for the treatment of UEDVT, studies have repeatedly shown that many patients with UEDVT do not receive anticoagulation: 56% of 300 cases in a peripheral vascular lab [40] and 20% of 94 cases in an academic center [84]. A bleeding risk was not frequently documented in the patients who did not receive anticoagulation.

Endovascular therapy (thrombolysis, thrombectomy, and stenting) should be used in selected cases only.

Thrombolysis Small retrospective studies have shown that catheter directed thrombolysis [85,86], mechanical thrombectomy [87], and techniques using both mechanical and catheter directed thrombolysis [88-90], were safe, with varying levels of effectiveness. The 2012 ACCP guidelines recommend thrombolysis in patients who fulfill the current criteria: severe and recent symptoms, extensive thrombus, low bleeding risk, and good functional status and life expectancy [1].

Superior vena cava filter placement for patients with contraindication to anticoagulation can be used off-label. Its safety and effectiveness were demonstrated in small studies in which the procedure related complication rate (misplacement or migration of the filter, caval occlusion, pneumothorax, pulmonary embolism) was low. The overall mortality rate was high given the patients' comorbidities [91,92].

Decompression surgery in the thoracic outlet syndrome: First rib resection with scalenectomy decompresses the thoracic outlet. It was found in small studies to decrease the long-term disability related to the PTS. Delay in surgery was associated with worse outcomes [93-96].

Special circumstances/population

Screening of asymptomatic upper extremities was shown to be ineffective [97] and is therefore not indicated.

An UEDVT distal to the axillary vein i.e. in the brachial vein has a probably lower risk of complications compared to an UEDVT at or central to the axillary vein. Anticoagulation might cause an unjustified risk of bleeding. Clinical or ultrasound surveillance to detect the extension of the UEDVT, prophylactic anticoagulation, or shorter duration of anticoagulation (less than 3 months) might be acceptable alternatives. The ACCP favors anticoagulation in cases that are symptomatic, associated with a central line that will remain in place, or associated with cancer in the absence of central venous lines, all in the absence of a bleeding risk [1].

When to get a thrombophilic work-up?

UEDVT is less associated with hereditary thrombophilia than LEDVT. Studies have tried to identify subgroups of patients in whom testing might be cost effective and would result in the extension of the anticoagulation duration. In women taking oral contraceptives, a synergistic association between primary UEDVT and hereditary thrombophilia, mainly prothrombin G20210A, was found in 2 case-control studies [37,98].

Patients with upper & lower extremity DVT

The coexistence of upper and lower extremity is high: 21% of the 211 patients diagnosed with UEDVT were positive for acute LEDVT on ultrasound [99]. An earlier small study by the same authors had showed that patients with a combined upper and lower extremity DVT had higher mortality, despite the same risk of PE, probably due to more severe illness [100].

Post-shoulder replacement UEDVT

Contrary to previous data [101], recent data, including results from the RECOS registry(102), is reporting very low (less than 1%) post-shoulder replacement VTE [103,104]. Systematic VTE prophylaxis is therefore not recommended after shoulder replacement and should be reserved for selected cases only.

Quality Improvement and Cost-effective Strategies

Prevention of hospital-acquired VTE has been the focus of different quality groups and societies, given its high mortality, morbidity and financial burden. The VTE core measure [105] and the Patient Safety Indicator (PSI) # 12 [106] are the main public quality metrics that are now reported by most hospitals. In a level-one trauma center, the introduction of smaller triple lumen and the preferential usage of single lumen PICC lines decreased the risk of UEDVT. Each prevented event saved $15973 and avoided a 4.6 days increase in the length of stay [58]. The introduction of a process that standardized the requests for PICC lines in McGill University Centre lead to an overall savings of approximately 1.1 Million in around 8 months [107].

Controversies and Cutting Edge

The New Oral Anticoagulants are currently being used for the treatment of UEDVT, by extrapolation from their use in the therapy of LEDVT. They however need to be studied in the treatment (and prophylaxis) of UEDVT. Currently, one ongoing study is addressing the problem: A Pilot Study in Cancer Patients With Central Venous Catheter Associated Deep Vein Thrombosis in the Upper Extremity Treated With Rivaroxaban (Catheter 2) http://ClinicalTrials.gov/show/NCT01708850.

Prophylaxis: While pharmacological prophylaxis is not currently indicated to prevent CVC associated UEDVT, many studies show benefit, especially in high-risk patients, mainly cancer patients. Further studies will be needed to identify subgroups in which prophylaxis is indicated.

Treatment: Major randomized controlled trials in the treatment of UEDVT are needed, as the extrapolation from lower extremity DVT data might not be accurate.

Summary

UEDVT is to be taken as seriously as lower extremity DVT given its frequency and high mortality.

CVC are the main risk factor. Appropriate ordering and usage of CVC are keys for UEDVT prevention.

Primary UEDVT, mainly due to the Paget-Schroetter syndrome is infrequent. Upon diagnosis, a surgery referral is primordial in preventing future disability.

Despite the poor data, anticoagulation of acute UEDVT is indicated.

Research is needed in the areas of prophylaxis and treatment, including the role of the new oral anticoagulants.

Case Conclusions

Case 1

Upon evaluation, the patient denied pain in the right upper extremity. On examination, she had normal vitals and no edema, erythema or tenderness of the right upper extremity. The attending physician ordered an ultrasound of the extremity. He asked the nurse to flush the line with t-PA (alteplase). The t-PA restored the function of the line. The ultrasound showed an acute thrombus of the brachial and axillary veins.

The attending physician considered starting an oral direct factor Xa inhibitor but he ended up choosing enoxaparin as a bridge to warfarin, given the lack of trials supporting the use of the new oral anticoagulants in the treatment of UEDVT. He asked the nurse not to pull the PICC line since it is functioning and clinically needed for 5 more days. He planned on reminding his colleague upon sign out to pull the line as soon as the intravenous antibiotherapy was finished. He notified the patient's primary care physician about the plan to continue the warfarin for 3 months.

Case 2

The patient was not febrile and did not have an elevated white count. The ER team suspected an UEDVT and ordered an ultrasound that came back normal. She was therefore admitted to the hospital for antibiotic therapy of a possible cellulitis. More than 24 hours later, there was no improvement. The Hospitalist team was concerned about a falsely negative initial ultrasound. Ddimer level was checked and was found to be markedly abnormal. A repeat ultrasound this time revealed a small subclavian thrombus.

A heparin drip was immediately started. Vascular surgery recommended against thrombolysis given the lack of convincing data about its usefulness in preventing the post-thrombotic syndrome, especially when the thrombus is small. The Paget-Schroetter syndrome was suspected so the Hospitalist team called thoracic surgery. A hematology specialist discussed with the patient the potential benefit of getting a thrombophilic work-up based on small studies showing higher levels of thrombophilia in women getting a primary UEDVT while on oral contraceptives.

References

1. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, et al. (2012) Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 141: e419S-94S.
2. Héron E, Lozinguez O, Alhenc-Gelas M, Emmerich J, Fiessinger JN (2000) Hypercoagulable states in primary upper-extremity deep vein thrombosis. Arch Intern Med 160: 382-386.
3. Isma N, Svensson PJ, Gottsäter A, Lindblad B (2010) Upper extremity deep venous thrombosis in the population-based Malmö thrombophilia study (MATS). Epidemiology, risk factors, recurrence risk, and mortality. Thromb Res 125: e335-338.
4. Spencer FA, Emery C, Lessard D, Goldberg RJ; Worcester Venous Thromboembolism Study (2007) Upper extremity deep vein thrombosis: a community-based perspective. Am J Med 120: 678-684.
5. Winters JP, Callas PW, Cushman M, Repp AB, Zakai NA (2015) Central venous catheters and upper extremity deep vein thrombosis in medical inpatients: the Medical Inpatients and Thrombosis (MITH) Study. J Thromb Haemost .
6. Khanna R, Maynard G, Sadeghi B, Hensley L, Medvedev S, et al. (2014) Incidence of hospital-acquired venous thromboembolic codes in medical patients hospitalized in academic medical centers. J Hosp Med;9:221-225.
7. Lamontagne F, McIntyre L, Dodek P, Heels-Ansdell D, Meade M, et al. (2014) Nonleg venous thrombosis in critically ill adults: a nested prospective cohort study. JAMA Intern Med 174: 689-696.
8. Muñoz FJ, Mismetti P, Poggio R, Valle R, Barrón M, et al. (2008) Clinical outcome of patients with upper-extremity deep vein thrombosis: results from the RIETE Registry. Chest 133: 143-148.
9. Hingorani A, Ascher E, Lorenson E, DePippo P, Salles-Cunha S, et al. (1997) Upper extremity deep venous thrombosis and its impact on

morbidity and mortality rates in a hospital-based population. J Vasc Surg 26: 853-860.

10. Flinterman LE, Van Hylckama Vlieg A, Rosendaal FR, Doggen CJ (2008) Recurrent thrombosis and survival after a first venous thrombosis of the upper extremity. Circulation 118: 1366-1372.
11. Lechner D, Wiener C, Weltermann A, Eischer L, Eichinger S, et al. (2008) Comparison between idiopathic deep vein thrombosis of the upper and lower extremity regarding risk factors and recurrence. J Thromb Haemost 6: 1269-1274.
12. Joffe HV, Kucher N, Tapson VF, Goldhaber SZ; Deep Vein Thrombosis (DVT) FREE Steering Committee (2004) Upper-extremity deep vein thrombosis: a prospective registry of 592 patients. Circulation 110: 1605-1611.
13. Blom JW, Doggen CJ, Osanto S, Rosendaal FR (2005) Old and new risk factors for upper extremity deep venous thrombosis. J Thromb Haemost 3: 2471-2478.
14. Timsit JF, Farkas JC, Boyer JM, Martin JB, Misset B, et al. (1998) Central vein catheter-related thrombosis in intensive care patients: incidence, risks factors, and relationship with catheter-related sepsis. Chest 114: 207-213.
15. Wu X, Studer W, Skarvan K, Seeberger MD (1999) High incidence of intravenous thrombi after short-term central venous catheterization of the internal jugular vein. J Clin Anesth 11: 482-485.
16. Yeral M, Boga C, Oguzkurt L, Asma S, Kasar M, et al. (2014) Short-term central venous catheter complications in patients with sickle cell disease who undergo apheresis. J Thromb Thrombolysis 37: 97-101.
17. Grisariu S, Spectre G, Kalish Y, Gatt ME (2013) Increased risk of central venous catheter-associated thrombosis in acute promyelocytic leukemia: a single-institution experience. Eur J Haematol; 90: 397-403.
18. Guillet S, Zeller V2, Dubée V,Ducroquet F3, Desplaces N, et al. (2015) Central venous catheter thrombosis during intravenous antibiotic therapy: results of a large cohort study. Antimicrob Agents Chemother .
19. Wilson TJ, Stetler WR, Jr., Fletcher JJ. (2013) Comparison of catheter-related large vein thrombosis in centrally inserted versus peripherally inserted central venous lines in the neurological intensive care unit. Clin Neurol Neurosurg; 115: 879-882.
20. Chopra V, Anand S, Hickner A, Buist M, Rogers MA, et al. (2013) Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. Lancet 382: 311-325.
21. Leroyer C, Lashéras A, Marie V, Le Bras Y, Carteret T, et al. (2013) Prospective follow-up of complications related to peripherally inserted central catheters. Med Mal Infect 43: 350-355.
22. Xing L, Adhikari VP, Liu H, Kong LQ, Liu SC, et al. (2012) Diagnosis prevention and treatment for PICC-related upper extremity deep vein thrombosis in breast cancer patients. Asia Pac J Clin Oncol 8: e12-16.
23. Liem TK, Yanit KE, Moseley SE, Landry GJ, Deloughery TG, Rumwell CA, et al. (2012) Peripherally inserted central catheter usage patterns and associated symptomatic upper extremity venous thrombosis. J Vasc Surg; 55: 761-767.
24. Patel GS, Jain K, Kumar R, Strickland AH, Pellegrini L, et al. (2007) Comparison of peripherally inserted central venous catheters (PICC) versus subcutaneously implanted port-chamber catheters by complication and cost for patients receiving chemotherapy for non-haematological malignancies. Support Care Cancer;22: 121-128.
25. Lim MY, Al-Kali A, Ashrani AA, Begna KH, Elliott MA, et al. (2013) Comparison of complication rates of Hickman((R)) catheters versus peripherally inserted central catheters in patients with acute myeloid leukemia undergoing induction chemotherapy. Leuk Lymphoma; 54:1263-1267.
26. Anderson AJ, Krasnow SH, Boyer MW, Cutler DJ, Jones BD, et al. (1989) Thrombosis: the major Hickman catheter complication in patients with solid tumor. Chest 95: 71-75.
27. Da Costa SS, Neto AS, Costa R, Caldas JG, Filho MM, (2002) Incidence and risk factors of upper extremity deep vein lesions after permanent transvenous pacemaker implant: a 6-month follow-up prospective study. Pacing Clin Electrophysiol;25:1301-1306.
28. Girolami A, Prandoni P, Zanon E, Bagatella P, Girolami B (1999) Venous thromboses of upper limbs are more frequently associated with occult cancer as compared with those of lower limbs. Blood Coagul Fibrinolysis; 10: 455-457.
29. Marnejon T, Angelo D, Abu Abdou A, Gemmel D (2012) Risk factors for upper extremity venous thrombosis associated with peripherally inserted central venous catheters. J Vasc Access 13: 231-238.
30. Daneschvar HL, Seddighzadeh A, Piazza G, Goldhaber SZ (2008) Deep vein thrombosis in patients with chronic kidney disease. Thromb Haemost 99: 1035-1039.
31. Del Principe MI, Buccisano F, Maurillo L, Venditti D, Cefalo M, et al. (2013) Infections increase the risk of central venous catheter-related thrombosis in adult acute myeloid leukemia. Thromb Res 132: 511-514.
32. Ahn DH, Illum HB, Wang DH, Sharma A, Dowell JE. (2013) Upper extremity venous thrombosis in patients with cancer with peripherally inserted central venous catheters: a retrospective analysis of risk factors. J Oncol Pract; 9:e8-12.
33. Crowley AL, Peterson GE, Benjamin DK, Jr., Rimmer SH, Todd C, et al. (2008) Venous thrombosis in patients with short- and long-term central venous catheter-associated Staphylococcus aureus bacteremia. Crit Care Med; 36:385-390.
34. Linnemann B, Meister F, Schwonberg J, Schindewolf M, Zgouras D, et al. (2008) Hereditary and acquired thrombophilia in patients with upper extremity deep-vein thrombosis. Results from the MAISTHRO registry. Thromb Haemost 100: 440-446.
35. Gabriel F, Portolés O, Labiós M, Rodríguez C, Cisneros E, et al. (2013) Usefulness of thrombophilia testing in venous thromboembolic disease: findings from the RIETE registry. Clin Appl Thromb Hemost 19: 42-47.
36. Riordan M, Weiden PL (1998) Factor V Leiden mutation does not account for central venous catheter-related thrombosis. Am J Hematol 58: 150-152.
37. Martinelli I, Battaglioli T, Bucciarelli P, Passamonti SM, Mannucci PM (2004) Risk factors and recurrence rate of primary deep vein thrombosis of the upper extremities. Circulation 110: 566-570.
38. Arnhjort T, Nordberg J, Delle M, Borgis CJ, Rosfors S, et al. (2014) The importance of the costoclavicular space in upper limb primary deep vein thrombosis, a study with magnetic resonance imaging (MRI) technique enhanced by a blood pool agent. Eur J Intern Med; 25:545-549.
39. Gharagozloo F, Meyer M, Tempesta B, Strother E, Margolis M, et al. (2012) Proposed pathogenesis of Paget-Schroetter disease: impingement of the subclavian vein by a congenitally malformed bony tubercle on the first rib. J Clin Pathol 65: 262-266.
40. Levy MM, Albuquerque F, Pfeifer JD (2012) Low incidence of pulmonary embolism associated with upper-extremity deep venous thrombosis. Ann Vasc Surg 26: 964-972.
41. Luciani A, Clement O, Halimi P, Goudot D, Portier F, et al. (2001) Catheter-related upper extremity deep venous thrombosis in cancer patients: a prospective study based on Doppler US. Radiology 220: 655-660.
42. De Cicco M, Matovic M, Balestreri L, Panarello G, Fantin D, et al. (1997) Central venous thrombosis: an early and frequent complication in cancer patients bearing long-term silastic catheter. A prospective study. Thromb Res 86: 101-113.
43. Marinella MA,Kathula SK, Markert RJ (2000) Spectrum of upper-extremity deep venous thrombosis in a community teaching hospital. Heart Lung 29: 113-117.
44. Oymak FS, Buyukoglan H, Tokgoz B, Ozkan M, Tasdemir K, et al. (2005) Prevalence of thromboembolic disease including superior vena cava and brachiocephalic veins.Clin Appl Thromb Hemost 11: 183-189.
45. Constans J, Salmi LR, Sevestre-Pietri MA, Perusat S, Nguon M, et al. (2008) A clinical prediction score for upper extremity deep venous thrombosis. Thromb Haemost 99: 202-207.
46. Prandoni P, Bernardi E, Marchiori A, Lensing AW, Prins MH, et al. (2004) The long term clinical course of acute deep vein thrombosis of the arm: prospective cohort study. BMJ 329: 484-485.

47. Persson LM, Arnhjort T, Lärfars G, Rosfors S (2006) Hemodynamic and morphologic evaluation of sequelae of primary upper extremity deep venous thromboses treated with anticoagulation. J Vasc Surg 43: 1230-1235.
48. Kahn SR (2009) Measurement properties of the Villalta scale to define and classify the severity of the post-thrombotic syndrome. J Thromb Haemost 7: 884-888.
49. Berzaczy D, Popovic M, Reiter M, Puchner S, Weber M, et al. (2010) Quality of life in patients with idiopathic subclavian vein thrombosis. Thromb Res 125: 25-28.
50. Di Nisio M, Van Sluis GL, Bossuyt PM, Büller HR, Porreca E, et al. (2010) Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. J Thromb Haemost 8: 684-692.
51. Knudson GJ, Wiedmeyer DA, Erickson SJ, Foley WD, Lawson TL, et al. (1990) Color Doppler sonographic imaging in the assessment of upper-extremity deep venous thrombosis. AJR Am J Roentgenol 154: 399-403.
52. Merminod T, Pellicciotta S, Bounameaux H (2006) Limited usefulness of D-dimer in suspected deep vein thrombosis of the upper extremities. Blood Coagul Fibrinolysis 17: 225-226.
53. Moriarty JM, Bandyk DF2, Broderick DF3, Cornelius RS4, Dill KE5, et al. (2015) ACR Appropriateness Criteria Imaging in the Diagnosis of Thoracic Outlet Syndrome. J Am Coll Radiol 12: 438-443.
54. Baarslag HJ, Van Beek EJ, Reekers JA (2004) Magnetic resonance venography in consecutive patients with suspected deep vein thrombosis of the upper extremity: initial experience. Acta Radiol 45: 38-43.
55. Kleinjan A, Di Nisio M, Beyer-Westendorf J, Camporese G, Cosmi B, et al. (2014) Safety and feasibility of a diagnostic algorithm combining clinical probability, d-dimer testing, and ultrasonography for suspected upper extremity deep venous thrombosis: a prospective management study. Ann Intern Med; 160:451-457.
56. Di Nisio M, Peinemann F, Porreca E, Rutjes AW (2015) Treatment for superficial infusion thrombophlebitis of the upper extremity. Cochrane Database Syst Rev 11: CD011015.
57. Likes K, Rochlin DH, Call D, Freischlag JA (2014) McCleery syndrome: etiology and outcome. Vasc Endovascular Surg 48: 106-110.
58. Evans RS,Sharp JH, Linford LH, Lloyd JF, Woller SC, et al. (2013) Reduction of peripherally inserted central catheter-associated DVT. Chest 143: 627-633.
59. Verso M, Agnelli G, Kamphuisen PW, Ageno W, Bazzan M, et al. (2008) Risk factors for upper limb deep vein thrombosis associated with the use of central vein catheter in cancer patients. Intern Emerg Med 3: 117-122.
60. Martin C, Viviand X, Saux P, Gouin F (1999) Upper-extremity deep vein thrombosis after central venous catheterization via the axillary vein. Crit Care Med 27: 2626-2629.
61. Li J, Fan YY, Xin MZ, Yan J, Hu W, et al. (2014) A randomised, controlled trial comparing the long-term effects of peripherally inserted central catheter placement in chemotherapy patients using B-mode ultrasound with modified Seldinger technique versus blind puncture. Eur J Oncol Nurs; 18:94-103.
62. Sperry BW, Roskos M, Oskoui R (2012) The effect of laterality on venous thromboembolism formation after peripherally inserted central catheter placement. J Vasc Access 13: 91-95.
63. Biffi R, Orsi F, Pozzi S, Pace U, Bonomo G, et al. (2009) Best choice of central venous insertion site for the prevention of catheter-related complications in adult patients who need cancer therapy: a randomized trial. Ann Oncol; 20:935-940.
64. Akl EA, Ramly EP, Kahale LA, Yosuico VE, Barba M, et al. (2014) Anticoagulation for people with cancer and central venous catheters. Cochrane Database Syst Rev; 10:CD006468.
65. Jonker MA, Osterby KR, Vermeulen LC, Kleppin SM, Kudsk KA (2010) Does low-dose heparin maintain central venous access device patency?: a comparison of heparin versus saline during a period of heparin shortage. JPEN J Parenter Enteral Nutr 34: 444-449.
66. Uslu S, Ozdemir H, Comert S, Bolat F, Nuhoglu A. (2010) The effect of low-dose heparin on maintaining peripherally inserted percutaneous central venous catheters in neonates. J Perinatol; 30:794-799.
67. Shah PS, Kalyn A, Satodia P, Dunn MS, Parvez B, et al. (2007) A randomized, controlled trial of heparin versus placebo infusion to prolong the usability of peripherally placed percutaneous central venous catheters (PCVCs) in neonates: the HIP (Heparin Infusion for PCVC) study. Pediatrics 119: e284-291.
68. Abdelkefi A, Ben Othman T, Kammoun L, Chelli M, Romdhane NB, et al. (2004) Prevention of central venous line-related thrombosis by continuous infusion of low-dose unfractionated heparin, in patients with haemato-oncological disease. A randomized controlled trial. Thromb Haemost 92: 654-661.
69. Anton N, Cox PN, Massicotte MP, Chait P, Yasui Y, et al. (2009) Heparin-bonded central venous catheters do not reduce thrombosis in infants with congenital heart disease: a blinded randomized, controlled trial. Pediatrics;123:e453-458.
70. Pierce CM, Wade A, Mok Q (2000) Heparin-bonded central venous lines reduce thrombotic and infective complications in critically ill children. Intensive Care Med 26: 967-972.
71. Krafte-Jacobs B, Sivit CJ, Mejia R, Pollack MM (1995) Catheter-related thrombosis in critically ill children: comparison of catheters with and without heparin bonding. J Pediatr 126: 50-54.
72. Malinoski DJ, Ewing T, Patel MS, Nguyen D, Le T, et al. (2011) The natural history of upper extremity deep venous thromboses in critically ill surgical and trauma patients: what is the role of anticoagulation? J Trauma 71: 316-321.
73. Jones MA, Lee DY, Segall JA, Landry GJ, Liem TK, et al. (2010) Characterizing resolution of catheter-associated upper extremity deep venous thrombosis. J Vasc Surg 51: 108-113.
74. Kenney BD, David M, Bensoussan AL (1996) Anticoagulation without catheter removal in children with catheter-related central vein thrombosis. J Pediatr Surg 31: 816-818.
75. Gabrail N, Sandler E, Charu V, Anas N, Lim E, et al. (2010) TROPICS 1: a phase III, randomized, double-blind, placebo-controlled study of tenecteplase for restoration of function in dysfunctional central venous catheters.J Vasc Interv Radiol 21: 1852-1858.
76. Svoboda P, Barton RP, Barbarash OL, Butylin AA, Jacobs BR, Lata J, et al. (2004) Recombinant urokinase is safe and effective in restoring patency to occluded central venous access devices: a multiple-center, international trial. Crit Care Med; 32:1990-1996.
77. Schindler J, Bona RD, Chen HH, Feingold JM, Edwards RL, et al. (1999) Regional thrombolysis with urokinase for central venous catheter-related thrombosis in patients undergoing high-dose chemotherapy with autologous blood stem cell rescue. Clin Appl Thromb Hemost; 5:25-29.
78. Liu CY, Jain V, Shields AF, Heilbrun LK (2004) Efficacy and safety of reteplase for central venous catheter occlusion in patients with cancer. J Vasc Interv Radiol 15: 39-44.
79. Semba CP, Deitcher SR, Li X, Resnansky L, Tu T, et al. (2002) Treatment of occluded central venous catheters with alteplase: results in 1,064 patients. J Vasc Interv Radiol 13: 1199-1205.
80. Ponec D, Irwin D, Haire WD, Hill PA, Li X, et al. (2001) Recombinant tissue plasminogen activator (alteplase) for restoration of flow in occluded central venous access devices: a double-blind placebo-controlled trial--the Cardiovascular Thrombolytic to Open Occluded Lines (COOL) efficacy trial. J Vasc Interv Radiol; 12: 951-955.
81. Ernst FR, Chen E, Lipkin C, Tayama D, Amin AN. (2014) Comparison of hospital length of stay, costs, and readmissions of alteplase versus catheter replacement among patients with occluded central venous catheters. J Hosp Med; 9:490-496.
82. Rathbun SW, Stoner JA, Whitsett TL (2011) Treatment of upper-extremity deep vein thrombosis. J Thromb Haemost 9: 1924-1930.
83. Savage KJ, Wells PS, Schulz V, Goudie D, Morrow B, et al. (1999) Outpatient use of low molecular weight heparin (Dalteparin) for the treatment of deep vein thrombosis of the upper extremity. Thromb Haemost 82: 1008-1010.

84. Lee JA, Zierler BK, Zierler RE (2012) The risk factors and clinical outcomes of upper extremity deep vein thrombosis. Vasc Endovascular Surg 46: 139-144.
85. Vik A, Holme PA, Singh K, Dorenberg E, Nordhus KC, et al. (2009) Catheter-directed thrombolysis for treatment of deep venous thrombosis in the upper extremities.Cardiovasc Intervent Radiol 32: 980-987.
86. Sabeti S, Schillinger M, Mlekusch W, Haumer M, Ahmadi R, et al. (2002) Treatment of subclavian-axillary vein thrombosis: long-term outcome of anticoagulation versus systemic thrombolysis. Thromb Res 108: 279-285.
87. Arko FR, Davis CM 3rd, Murphy EH, Smith ST, Timaran CH, et al. (2007) Aggressive percutaneous mechanical thrombectomy of deep venous thrombosis: early clinical results. Arch Surg 142: 513-518.
88. Chaudhry MA, Pappy R, Hennebry TA (2013) Use of the trellis device in the management of deep vein thrombosis: a retrospective single-center experience. J Invasive Cardiol 25: 296-299.
89. Kim HS, Patra A, Paxton BE, Khan J, Streiff MB (2006) Catheter-directed thrombolysis with percutaneous rheolytic thrombectomy versus thrombolysis alone in upper and lower extremity deep vein thrombosis. Cardiovasc Intervent Radiol 29: 1003-1007.
90. Parikh S, Motarjeme A, McNamara T, Raabe R, Hagspiel K, et al. (2008) Ultrasound-accelerated thrombolysis for the treatment of deep vein thrombosis: initial clinical experience. J Vasc Interv Radiol 19: 521-528.
91. Usoh F, Hingorani A, Ascher E, Shiferson A, Tran V, et al. (2009) Long-term follow-up for superior vena cava filter placement. Ann Vasc Surg 23: 350-354.
92. Spence LD, Gironta MG, Malde HM, Mickolick CT, Geisinger MA, et al. (1999) Acute upper extremity deep venous thrombosis: safety and effectiveness of superior vena caval filters. Radiology 210: 53-58.
93. Taylor JM, Telford RJ, Kinsella DC, Watkinson AF, Thompson JF (2013) Long-term clinical and functional outcome following treatment for Paget-Schroetter syndrome. Br J Surg 100: 1459-1464.
94. Chang K, Graf E, Davis K, Demos J, Roethle T, et al. (2011) Spectrum of thoracic outlet syndrome presentation in adolescents. Arch Surg 146: 1383-1387.
95. Melby SJ, Vedantham S, Narra VR, Paletta GA, Jr., Khoo-Summers L, et al. (2008) Comprehensive surgical management of the competitive athlete with effort thrombosis of the subclavian vein (Paget-Schroetter syndrome). J Vasc Surg; 47:809-20; discussion 21.
96. Fassiadis N, Roidl M, South M (2005) Are we managing primary upper limb deep venous thrombosis aggressively enough in the district? Int Angiol 24: 255-257.
97. Spaniolas K, Velmahos GC, Wicky S, Nussbaumer K, Petrovick L, et al. (2008) Is upper extremity deep venous thrombosis underdiagnosed in trauma patients? Am Surg 74: 124-128.
98. Vayá A, Mira Y, Mateo J, Falco C, Villa P, et al. (2003) Prothrombin G20210A mutation and oral contraceptive use increase upper-extremity deep vein thrombotic risk. Thromb Haemost 89: 452-457.
99. Hingorani AP, Ascher E, Markevich N, Schutzer RW, Kallakuri S, et al. (2006) Prospective evaluation of combined upper and lower extremity DVT. Vasc Endovascular Surg 40: 131-134.
100. Hingorani A, Ascher E, Ward M, Mazzariol F, Gunduz Y, et al. (2001) Combined upper and lower extremity deep venous thrombosis. Cardiovasc Surg 9: 472-477.
101. Willis AA, Warren RF, Craig EV, Adler RS, Cordasco FA, et al. (2009) Deep vein thrombosis after reconstructive shoulder arthroplasty: a prospective observational study. J Shoulder Elbow Surg; 18:100-106.
102. Imberti D, Ivaldo N2, Murena L3, Paladini P4, Castagna A5, et al. (2014) Venous thromboembolism in patients undergoing shoulder surgery: findings from the RECOS Registry. Thromb Res 134: 273-277.
103. Hastie GR, Pederson A, Redfern D. (2014) venous thromboembolism incidence in upper limb orthopedic surgery: do these procedures increase venous thromboembolism risk? J Shoulder Elbow Surg; 23:1481-1484.
104. Day JS, Ramsey ML2, Lau E3, Williams GR4 (2015) Risk of venous thromboembolism after shoulder arthroplasty in the Medicare population. J Shoulder Elbow Surg 24: 98-105.
105. http://www.jointcommission.org/venous_thromboembolism/
106. http://www.qualityindicators.ahrq.gov/Downloads/Modules/PSI/V44/TechSpecs/PSI%2012%20Postoperative%20PE%20or%20DVT%20Rate.pdf.
107. O'Brien J, Paquet F, Lindsay R, Valenti D (2013) Insertion of PICCs with minimum number of lumens reduces complications and costs. J Am Coll Radiol 10: 864-868.
108. Mino JS, Gutnick JR, Monteiro R, Anzlovar N, Siperstein AE. (2014) Line-associated thrombosis as the major cause of hospital-acquired deep vein thromboses: an analysis from National Surgical Quality Improvement Program data and a call to reassess prophylaxis strategies. Am J Surg; 208:45-49.
109. Hingorani A, Ascher E, Markevich N, Yorkovich W, Schutzer R, et al. (2005) Risk factors for mortality in patients with upper extremity and internal jugular deep venous thrombosis. J Vasc Surg 41: 476-478.
110. Kooij JD, Van der Zant FM, van Beek EJ, Reekers JA (1997) Pulmonary embolism in deep venous thrombosis of the upper extremity: more often in catheter-related thrombosis. Neth J Med 50: 238-242.
111. Kang J, Sun W,Li H,Ma E,Wang K,et al. (2015) Peripherally inserted central catheter-related vein thrombosis in breast cancer patients. J Vasc Access 0: 0.
112. Kang JR, Long LH,Yan SW,Wei WW2, Jun HZ2, et al. (2015) Peripherally Inserted Central Catheter-Related Vein Thrombosis in Patients With Lung Cancer. Clin Appl Thromb Hemost .
113. Austin RE, Shahrokhi S, Bolourani S, Jeschke MG (2015) Peripherally inserted central venous catheter safety in burn care: a single-center retrospective cohort review. J Burn Care Res 36: 111-117.
114. Chopra V, Ratz D, Kuhn L, Lopus T, Lee A, et al. (2014) Peripherally inserted central catheter-related deep vein thrombosis: contemporary patterns and predictors. J Thromb Haemost; 12:847-854.
115. Itkin M, Mondshein JI, Stavropoulos SW, Shlansky-Goldberg RD, Soulen MC, et al. (2014) Peripherally inserted central catheter thrombosis--reverse tapered versus nontapered catheters: a randomized controlled study. J Vasc Interv Radiol; 25:85-91 e1.
116. Aw A, Carrier M, Koczerginski J, McDiarmid S, Tay J (2012) Incidence and predictive factors of symptomatic thrombosis related to peripherally inserted central catheters in chemotherapy patients. Thromb Res 130: 323-326.
117. Wilson TJ, Brown DL, Meurer WJ, Stetler WR Jr, Wilkinson DA, et al. (2012) Risk factors associated with peripherally inserted central venous catheter-related large vein thrombosis in neurological intensive care patients. Intensive Care Med; 38:272-278.
118. Tran H, Arellano M, Chamsuddin A, Flowers C, Heffner LT, et al. (2010) Deep venous thromboses in patients with hematological malignancies after peripherally inserted central venous catheters. Leuk Lymphoma 51: 1473-1477.
119. Trerotola SO, Stavropoulos SW, Mondschein JI, Patel AA, Fishman N, et al. (2010) Triple-lumen peripherally inserted central catheter in patients in the critical care unit: prospective evaluation. Radiology 256: 312-320.
120. Lobo BL, Vaidean G, Broyles J, Reaves AB, Shorr RI (2009) Risk of venous thromboembolism in hospitalized patients with peripherally inserted central catheters. J Hosp Med 4: 417-422.
121. Periard D, Monney P, Waeber G, Zurkinden C, Mazzolai L, et al. (2008) Randomized controlled trial of peripherally inserted central catheters vs. peripheral catheters for middle duration in-hospital intravenous therapy. J Thromb Haemost; 6:1281-1288.
122. Abdullah BJ, Mohammad N, Sangkar JV, Abd Aziz YF, Gan GG, et al. (2005) Incidence of upper limb venous thrombosis associated with peripherally inserted central catheters (PICC). Br J Radiol 78: 596-600.
123. Allen AW, Megargell JL, Brown DB, Lynch FC, Singh H, et al. (2000) Venous thrombosis associated with the placement of peripherally inserted central catheters. J Vasc Interv Radiol 11: 1309-1314.
124. Grove JR,Pevec WC (2000) Venous thrombosis related to peripherally inserted central catheters. J Vasc Interv Radiol 11: 837-840.

125. Loughran SC, Borzatta M (1995) Peripherally inserted central catheters: a report of 2506 catheter days. JPEN J Parenter Enteral Nutr 19: 133-136.

126. Dal Molin A, Di Massimo DS, Braggion C, Bisogni S, Rizzi E, et al. (2012) Totally implantable central venous access ports in patients with cystic fibrosis: a multicenter prospective cohort study. J Vasc Access; 13:290-290.

127. Kriegel I, Cottu PH, Fourchotte V, Sanchez S, Fromantin I, et al. (2011) Wound healing and catheter thrombosis after implantable venous access device placement in 266 breast cancers treated with bevacizumab therapy. Anticancer Drugs; 22:1020-1023.

128. Yukisawa S, Fujiwara Y, Yamamoto Y, Ueno T, Matsueda K, et al. (2010) Upper-extremity deep vein thrombosis related to central venous port systems implanted in cancer patients. Br J Radiol 83: 850-853.

129. Lyon RD, Griggs KA, Johnson AM, Olsen JR (1999) Long-term follow-up of upper extremity implanted venous access devices in oncology patients. J Vasc Interv Radiol 10: 463-471.

130. Biffi R,Corrado F, de Braud F, de Lucia F, Scarpa D, et al. (1997) Long-term, totally implantable central venous access ports connected to a Groshong catheter for chemotherapy of solid tumours: experience from 178 cases using a single type of device. Eur J Cancer 33: 1190-1194.

131. Lavau-Denes S, Lacroix P, Maubon A, Preux PM, Genet D, et al. (2013) Prophylaxis of catheter-related deep vein thrombosis in cancer patients with low-dose warfarin, low molecular weight heparin, or control: a randomized, controlled, phase III study. Cancer Chemother Pharmacol 72: 65-73.

132. Bern MM, Lokich JJ, Wallach SR, Bothe A Jr, Benotti PN, et al. (1990) Very low doses of warfarin can prevent thrombosis in central venous catheters. A randomized prospective trial. Ann Intern Med 112: 423-428.

133. Brismar B, Hårdstedt C, Jacobson S, Kager L, Malmborg AS (1982) Reduction of catheter-associated thrombosis in parenteral nutrition by intravenous heparin therapy. Arch Surg 117: 1196-1199.

134. Young AM, Billingham LJ, Begum G, Kerr DJ, Hughes AI, et al. (2009) Warfarin thromboprophylaxis in cancer patients with central venous catheters (WARP): an open-label randomised trial. Lancet 373: 567-574.

135. Niers TM, Di Nisio M, Klerk CP, Baarslag HJ, Buller HR,et al. (2007) Prevention of catheter-related venous thrombosis with nadroparin in patients receiving chemotherapy for hematologic malignancies: a randomized, placebo-controlled study. J Thromb Haemost; 5:1878-1882.

136. Fagnani D, Franchi R, Porta C, Pugliese P, Borgonovo K, et al. (2007) Thrombosis-related complications and mortality in cancer patients with central venous devices: an observational study on the effect of antithrombotic prophylaxis. Ann Oncol; 18:551-555.

137. Karthaus M, Kretzschmar A, Kroning H, Biakhov M, Irwin D, et al. (2006) Dalteparin for prevention of catheter-related complications in cancer patients with central venous catheters: final results of a double-blind, placebo-controlled phase III trial. Ann Oncol; 17:289-296.

138. Verso M, Agnelli G, Bertoglio S, Di Somma FC, Paoletti F, et al. (2005) Enoxaparin for the prevention of venous thromboembolism associated with central vein catheter: a double-blind, placebo-controlled, randomized study in cancer patients. J Clin Oncol; 23: 4057-4062.

139. Couban S, Goodyear M, Burnell M, Dolan S, Wasi P, et al. (2005) Randomized placebo-controlled study of low-dose warfarin for the prevention of central venous catheter-associated thrombosis in patients with cancer. J Clin Oncol. 23:4063-4069.

140. Heaton DC, Han DY, Inder A (2002) Minidose (1 mg) warfarin as prophylaxis for central vein catheter thrombosis. Intern Med J 32: 84-88.

Study	Type	Number of patients	% UEDVT line related	Comment
Mino, J. S., et al. (2014).[108]	Retrospective	1857	95.20%	General surgery cases
Levy, M. M., et al. (2012).[40]	Retrospective	300	80%	Peripheral vascular laboratory
Lee, J. A., et al. (2012)[84]	Retrospective	373	93%	All patients underwent upper extremity duplex
Malinoski, D. J., et al. (2011).[72]	Prospective	129	64%	Surgical ICU, screening with ultrasound
Munoz, F. J., et al. (2008).[8]	Prospective	512	45%	Symptomatic, no systematic screening
Blom, J. W., et al. (2005). [13]	Retrospective	179	23%	
Hingorani, A., et al. (2005).[109]	Retrospective	546	60%	
Kooij, J. D., et al. (1997). [110]	Retrospective	78	53%	

Appendix 1: Percentage of patients with UEDVT that is associated with central lines or leads.

Study	Type of study	Number of patients or PICC lines	UEDVT incidence	Comment
Kang, J., et al. (2015). [111]	Retrospective	568 patients	1.40%	Breast cancer
Kang, J. R., et al. (2015). [112]	Retrospective	328 patients	5.20%	Lung cancer
Austin, R. E., et al. (2015).[113]	Retrospective	53 patients	5.50%	Hospitalized burn patients
Chopra, V., et al. (2014)[114]	Retrospective	966 PICC	3.4%, symptomatic	Risk factors: recent cancer diagnosis; PICC gauge
Itkin, M., et al. (2014)[115]	Prospective	332 patients	71.90%	Systematic screening
Leroyer, C., et al. (2013).[21]	Prospective	267 PICC	2.50%	Only 9% of lines used for chemotherapy
Ahn, D. H., et al. (2013)[32]	Retrospective	237 Patients	15%	Cancer patients

Lim, M. Y., et al. (2013). [25]	Retrospective	84 PICC	48.20%	Compared with 64 Hickman catheters (incidence thrombosis 3.2%). Leukemia patients
Aw, A., et al. (2012)[116]	Retrospective	340 patients	5.60%	
Liem, T. K., et al. (2012)[23]	Retrospective	2056 PICC	2.60%	
Wilson, T. J., et al. (2012)[117]	Retrospective	431PICC	8.40%	Neurologic ICU
				Symptomatic
Tran, H., et al. (2010).[118]	Retrospective	498 patients	7.8% symptomatic	Hem malignancies
		899 PICC		
Trerotola, S. O., et al. (2010). [119]	Prospective	50 patients	20% symptomatic	All PICC lines were triple lumen
			58% systematic ultrasound	
Lobo, B. L., et al. (2009).[120]	Retrospective	777 patients	4.89%	Symptomatic; hospitalized
Periard, D., et al. (2008).[121]	Randomized controlled trial	60 patients	20%	Hospitalized requiring at least 5 days of intravenous therapy
Abdullah, B. J., et al. (2005) [122]	Prospective	26 patients	38.50%	Venography screening
Allen, A. W., et al. (2000)[123]	Retrospective	119 patients	38%	Venography screening
Grove, J. R. and W. C. Pevec (2000)[124]	Retrospective	678 patients	3.90%	More thrombosis with larger lines
Loughran, S. C. and M. Borzatta (1995).[125]	Retrospective	322 PICC	<1%	Parenteral nutrition

Appendix 2: Incidence of PICC line associated UEDVT.

Study	Type	Number of patients or ports	Incidence of UEDVT	Comments
Dal Molin, A., et al. (2012). [126]	Prospective	80 patients	1.3%	Cystic fibrosis
Kriegel, I., et al. (2011)[127]	Non Randomized trial	273 ports on and 4196 ports not on bevacizumab	1.5% bevacizumab group; 1.2% control group	Metastatic breast cancer
Yukisawa, S., et al. (2010)[128]	Prospective	92 patients	73%; only 3% causing obstruction of venous flow	Chemotherapy for colorectal cancer, serial ultrasounds
Lyon, R. D., et al. (1999).[129]	Retrospective	204 patients	2.7%	Chemotherapy
Biffi, R., et al. (1997). [130]	Prospective	175 patients	1.12%	Cancer patients

Appendix 3: Incidence of Port associated UEDVT.

Study	Prophylaxis used
Lavau-Denes, S., et al. (2013)[131]	Low-molecular weight heparin, warfarin
Bern, M. M., et al. (1990).[132]	Very low doses of warfarin
Brismar, B., et al. (1982)[133]	Prophylactic dose of IV heparin

Appendix 4: Studies showing a favorable outcomes of chemoprophylaxis.

Marnejon, T., et al. (2012). [29]	Warfarin, Low-molecular weight heparin, unfractionated heparin

Young, A. M., et al. (2009).[134]	Warfarin
Niers, T. M., et al. (2007)[135]	Nadroparin
Fagnani, D., et al. (2007). [136]	Mainly low dose warfarin
Karthaus, M., et al. (2006).[137]	Dalteparin
Verso, M., et al. (2005). [138]	Enoxaparin
Couban, S., et al. (2005). [139]	1 mg warfarin
Heaton, D. C., et al. (2002).[140]	Mini dose warfarin

Appendix 5: Studies not showing a favorable outcome of chemoprophylaxis.