Cardiovascular medicine

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Critical review

Deep vein thrombosis: who still needs to be admitted?

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Abstract

Introduction

Since the introduction of low-molecular-weight heparins for safely treating deep vein thrombosis, outpatient treatment of this condition became a standard practice worldwide. Certain groups of patients were not represented in clinical trials of home treatment; however, they still need to be admitted. In deciding which patient to admit, physicians should take into account both comorbid clinical conditions and social, geographic and logistic constraints. Extension of venous thromboembolism (i.e., the presence of symptomatic pulmonary embolism, iliofemoral or caval thrombosis) and the risk of bleeding should also be included in the decision pathway. The aim of this critical review is to see if deep vein thrombosis can be treated at home or at hospital.

Conclusion

Deep vein thrombosis can be treated outside a hospital setting safely, but this varies between individuals. Some people need to be admitted into a hospital as there is a high risk of bleeding or relevant comorbidities.

It is advisable to implement clinical pathways to support the decision of safely assigning patients to outpatient management.

Introduction

Until the second half of 1990's, patients with deep vein thrombosis (DVT) needed to be admitted to a hospital and treated with intravenous unfractionated heparin for at least 5 days along with coumarins; this regimen requires close laboratory monitoring to be both effective and safe. Two landmark trials[1,2] showed that patients could be safely treated at home with low-molecular weight heparins, drugs that have proven effective when administered in fixed, weight-adjusted doses, one or two times a day without laboratory monitoring. Shortly afterwards, home treatment of DVT became a standard practice worldwide.

We recently revised more than 273,000 hospital discharge records across the last 8 years (2005–2012) in our Department, and we found that only a very small proportion of cases (0.083%) were discharged with an ICD-IX-CM code that led to an attribution to the Diagnosis Related Group 128 (Cei M, unpublished data; Figure 1). Even if this exceptionally low value could be underestimated due to attribution of cases to other codes, we regard this as quite surprising. In fact, in clinical trials, many patients were excluded from home treatment, and outside the research context, physicians should have been even more cautious. We were therefore prompted to critically review the reasons that have led to patients being excluded from home treatment in clinical trials and the reasons that still suggest hospital admission for DVT patients. We focused on DVT of the lower limbs only in this review.

Discussion

The problem of exclusion from home treatment

In randomised clinical trials (RCT), a large proportion of eligible patients are excluded from home treatment: 1491/2230 (66.9%) in a study by Levine[1] and 216/692 (31.2%) in a trial by Koopman[2]. The proportion of excluded patients along with partial in-hospital initial treatment of those patients regarded as treated 'at home' were already identified as fundamental problems in a Cochrane review from Othieno[3]. This represents a clear lack of generalizability, the proportion of patients excluded from home treatment was not so high in

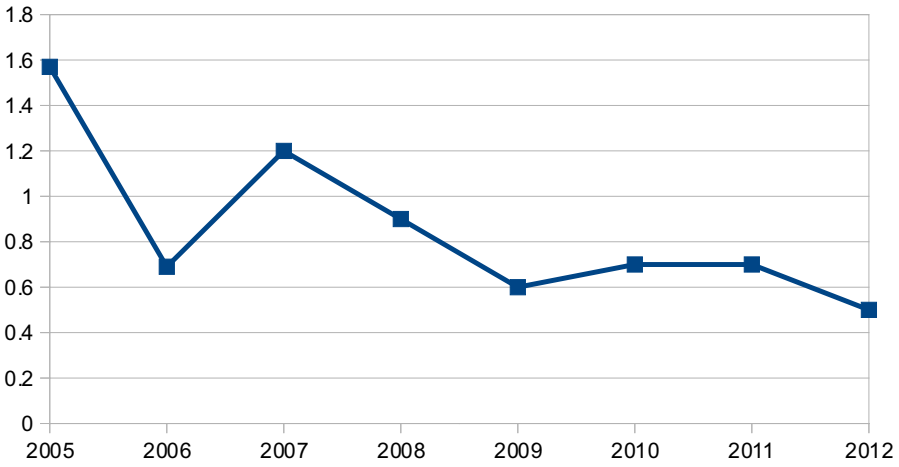

Figure 1: Hospital discharges for DTV at the Clinical Medicine Department, Livorno, Italy. Years 2005–2012 (number of cases per 1,000 discharges per year).

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many subsequent non-randomised studies[4–14], and current practices seem to be even more aggressive[15]. This could be due to, at least in part, the fact that study patients were excluded because of a wide range of conditions, some of which are peculiar to experimental context and are not usually considered in clinical practice (Table 1). On the other hand, a carefully designed pathway for outpatient treatment seems to be less permissive; up to 70% of patients were excluded from home treatment in a series from Shapiro[16]. Indeed, other exclusion reasons may include both conditions related to the clinical status of patients and those related to social, geographic and logistic constraints (Table 2). However, cancer (even when metastatic) should not be considered in itself a reason for exclusion from treatment at home[17]. Moreover, Hyers reported that home treatment was more common in suburban and rural areas than in urban settings in a large, multicentric study[18].

Table 1 Causes of exclusion from home treatment of DVT because of protocol demands

Lack of informed consent
Age < 18 years
Pregnancy or lactation
Previous venous thromboembolism
Treatment with heparins in the previous few days of enrolment
Reduced life expectancy

Table 2 Real-world cause of exclusion from home treatment of DVT

Clinical relevant PE
Extensive ilio-caval phlebothrombosis
Phlegmasia cerulea dolens
Active or recent bleeding
High risk of bleeding
Presence of comorbidities that require hospital admission
Allergy to heparin
History of heparin-induced thrombocytopenia
Geographic inaccessibility to follow-up
Likelihood of poor compliance
Hospital inadequate service

Table 3 The Hestia criteria for PE admission

If any of the following question is 'yes', then the patient should be admitted.
Is the patient haemodynamically unstable?
Is thrombolysis or embolectomy necessary?
Is there active bleeding or high risk for bleeding?
Is >24 hours of oxygen supply needed to maintain oxygen saturation >90%?
Is PE diagnosed during anticoagulant treatment?
Is there severe pain requiring intravenous pain medication for >24 hours?
Is there a medical or social reason for treatment in a hospital for >24 hours (infection, malignancy, no support system, etc.)?
Does the patient have a creatinine clearance of <30 mL/minute?
Does the patient have severe liver impairment?
Is the patient pregnant?
Does the patient have a documented history of heparin-induced thrombocytopenia?

Burden of venous thromboembolism

Approximately one third of DVT patients have some degree of pulmonary involvement[19], and trials have therefore included patients with pulmonary embolism (PE) that was not 'severe' or symptomatic. Moreover, the treatment of PE at home has been formally assessed[20]. Nowadays, we have been provided with a validated tool (the Hestia Criteria, Table 3) that safely identifies patients who do not need to be admitted for the management of PE[21]. Patients with extensive iliofemoral DVT or phlegmasia cerulea dolens, which are conditions that carry a high risk of severe post-thrombotic syndrome or those that require parenteral or opioid analgesia, were usually excluded from RCT, although they should been included. It may be reasonable to consider alternative strategies for these patients, including putting them on unfractionated heparin until they have been evaluated for surgical thrombectomy or catheter-directed thrombolysis[22,23]. Bilateral lower limb DVT should raise the suspect of inferior vena cava thrombosis and, in turn, possibly caval atresia[24], especially in the young; these patients should be therefore admitted for extensive evaluation and treatment.

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The fear of bleeding

Many patients in RCT are admitted because of active bleeding or the perceived high risk of bleeding. A miscellanea of clinical conditions have been considered to fulfil this criterion of exclusion, including the presence of bleeding diathesis (defined as thrombocytopenia < $100,000 \times 10^6$/L or INR > 1.4), uncontrolled or malignant hypertension, renal or hepatic failure (Figure 2), recent surgery (especially neurologic or ophthalmic) or lumbar puncture, recent gastrointestinal (within 1 month) or intracerebral bleeding (within 6 months) or the concomitant use of antiplatelet agents. To our knowledge, any formal score has never been adopted to exclude such patients from home treatment, and the decision to admit the patient usually relies largely on clinical judgement alone. Indeed, serious bleeding seems to be related more to the patient's characteristics than to the treatment setting[25], and bleeding risk tools have not been shown to be very accurate, at least in the elderly DVT patients[26].

Less well-defined causes of exclusion

Other causes of exclusion reported in Table 2 do not deserve specific comments, apart from the presence of comorbidities, which are the most frequently reported cause of hospital admission. As in the case of bleeding, this decision was left at the physician's discretion. Taken together, these two matters of exclusion lessen the strength of evidence in favour of the safety of home treatment, because the risk of an exclusion bias is not negligible.

Unresolved issues and concerns

It is unknown to what extent the real world follow-up consuetudes differ from the research context. In RCT, patients are more likely to be regularly followed by visiting nurses[27], have facilities to communicate with physicians responsible for the treatment and have the availability of fast-track hospital evaluation in case of symptoms. Clinical pathways should be assured to minimise the risk of outpatient treatment[28]. Standard practices may not be as effective in unrevealing DVT progression or assessing non-overt bleeding. In future, newer anticoagulants not needing laboratory monitoring would further increase the proportion of patients who will not seek medical advice during the period of active treatment.

Figure 2: Large leg haematoma in a woman with bilateral femoral DVT, low-risk PE and renal insufficiency.

Conclusion

Outpatient treatment of DVT is generally safe and effective, even when associated with low-risk PE. However, some patients should be admitted because of thromboembolic extension, high risk of bleeding or relevant comorbidities. It is advisable to implement clinical pathways to support the decision to safely assign a patient to outpatient management.

References

1. Levine M, Gent M, Hirsh J, Leclerc J, Anderson D, Weitz J, et al. A comparison of low-molecular weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep-vein thrombosis. N Engl J Med. 1996 Mar;334(11):677–81.

2. Koopman MM, Prandoni P, Piovella F, Ockelford PA, Brandjes DP, van der Meer J, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low-molecular-weight heparin administered at home. N Engl J Med. 1996 Mar;334(11):682–7.

3. Othieno R, Abu Affan M, Okpo E. Home versus in-patient treatment for deep vein thrombosis. Cochrane Database of Systematic Reviews. 2007, Issue 3. Art. No.: CD003076.

4. Harrison L, McGinnis J, Crowther M, Ginsberg J, Hirsh J. Assessment of outpatient treatment of deep-vein thrombosis and pulmonary embolism with low-molecular-weight heparin. Arch Intern Med. 1998 Oct;158(18):2001–3.

5. Grau E, Real E, Pastor E, Viciano V, Aguilò J. Home treatment of deep vein thrombosis: a two-years experience of a single institution. Haematologica. 1998 May;83(5):438–41.

6. Wells PS, Kovacs MJ, Bormanis J, Forgie MA, Goudie D, Morrow B, et al. Expanding eligibility for outpatient treatment of deep vein thrombosis and pulmonary embolism with low-molecular-weight

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heparin: a comparison of patients self-injection with homecare injection. Arch Intern Med. 1998 Sep;158(16):1809–12.
7. Ting SB, Ziegenbein RW, Gan TE, Catalano JV, Monagle P, Silvers J, et al. Dalteparin for deep venous thrombosis: a hospital-in-the-home program. Med J Aust. 1998 Mar;168(6):272–6.
8. Mattiasson I, Bernorp E, Bornhov S, Lagerstedt C, Lethagen S, Persson J, et al. Outpatient treatment of acute deep vein thrombosis. Int Angiol. 1998 Sep; 17(3):146–150.
9. O'Shaughnessy D, Miles J, Wimperis J. UK patients with deep vein thrombosis can be safely treated as out-patients. QJM. 2000 Oct;93(10):663–7.
10. Merli G, Spiro TE, Olsson CG, Abildgaard U, Davidson BL, Eldor A, et al. Subcutaneous Enoxaparin Once or Twice Daily Compared with Intravenous Unfractionated Heparin for Treatment of Venous Thromboembolic Disease. Ann Intern Med. 2001 Feb;134(3):191–202.
11. Schwarz T, Schmidt B, Höhlein U, Beyer J, Schröder HE, Schellong SM. Eligibility for home treatment of deep vein thrombosis: prospective study. BMJ. 2001 May;322(7296):1212–3.
12. Dunn AS, Schechter C, Gotlin A, Vornvolakis D, Jacobs E, Sacks HS, et al. Outpatient treatment of deep vein thrombosis in diverse inner-city patients. Am J Med 2001 Apr;110(6):458–62.
13. Schwarz T, Schmidt B, Beyer J, Schroder HE, Schellong SM. Eligibility for home treatment of deep vein thrombosis: a prospective study in 202 consecutive patients. J Vasc Surg. 2001 Dec;34(6):1065–70.
14. Chong BH, Brighton TA, Baker RI, Thurlow P, Lee CH, ASTH DVT Study Group. Once-daily enoxaparin in the outpatient setting versus unfractionated heparin in hospital for the treatment of symptomatic deep-vein thrombosis. J Thromb Thrombolysis. 2005 Jun;19(3):173–81.
15. Zidane M, van Hulsteijn LH, Brenninkmeijer BJ, Huisman MV. Out of hospital treatment with subcutaneous low molecular weight heparin in patients with acute deep-vein thrombosis: a prospective study in daily practice. Haematologica. 2006 Aug;91(8):1052–8.
16. Shapiro NI, Spear J, Sheehy S, Brown J, Edlow JA. Barriers to the use of outpatient enoxaparin therapy in patients with deep venous thrombosis. Am J Emerg Med. 2005 Jan;23(1):30–4.
17. Siragusa S, Arcara C, Malato A, Anastasio R, Valerio MR, Fulfaro F, et al. Home therapy for deep vein thrombosis and pulmonary embolism in cancer patients. Ann Oncol. 2005 May;16 Suppl 4:iv136–9.
18. Hyers TM, Spyropoulos AC, INNOVATE Investigators. Community-based treatment of venous thromboembolism with a low-molecular-weight heparin and warfarin. J Thromb Thrombolysis. 2007 Dec;24(3):225–32.
19. Stein PD, Matta F, Musani MH, Diaczok B. Silent Pulmonary Embolism in Patients with Deep Venous Thrombosis: A Systematic Review. Am J Med 2010 May;123(5):426–31.
20. Rodriguez-Cerrillo M, Alvarez-Arcaya A, Fernandez-Diaz E, Fernandez-Cruz A. A prospective study of the management of non-massive pulmonary embolism in the home. Eur J Intern Med. 2009 Oct;20(6):598–600.
21. Zondag W, Vingerhoets LM, Durian MF, Dolsma A, Faber LM, Hiddinga BI, et al. Hestia criteria can safely select patients with pulmonary embolism for outpatient treatment irrespective of right ventricular function. J Thromb Haemost. 2013.
22. Enden T, Haig Y, Klow NE, Slagsvold CE, Sandvik L, Ghanima W, et al. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. Lancet. 2012 Jan;379(9810):31–8.
23. Casey ET, Murad MH, Zumaeta-Garcia M, Elamin MB, Shi Q, Erwin PJ, et al. Treatment of acute iliofemoral deep vein thrombosis. J Vasc Surg. 2012 May;55(5):1463–73.
24. Lambert M, Marboeuf P, Midulla M, Trillot N, Beregi JP, Mounier-Vehier C, et al. Inferior vena cava agenesis and deep vein thrombosis: 10 patients and review of the literature. Vasc Med. 2010 Dec;15(6):451–9.
25. Nieto JA, Solano R, Ruiz-Ribò MD, Ruiz-Gimenez N, Prandoni P, Kearon C, et al. Fatal bleeding in patients receiving anticoagulant therapy for venous thromboembolism: findings from the RIETE registry. J Thromb Haemost. 2010 Jun;8(6):1216–22.
26. Scherz N, Méan M, Limacher A, Righini M, Jaeger K, Beer HJ, et al. Prospective, multicenter validation of prediction scores for major bleeding in elderly patients with venous thromboembolism. J Thromb Haemost. 2012 Dec.
27. Bishop B, Wilson AG, Post D, Howard L, Ruehlen L. A pilot study of home treatment of deep vein thrombosis with subcutaneous once-daily enoxaparin plus warfarin. J Manag Care Pharm. 2006 Jan–Feb;12(1):70–5.
28. Douketis JD. Treatment of deep vein thrombosis: what factors determine appropriate treatment? Can Fam Physician 2005 Feb;51:217–223.

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