

Venous thromboembolism, age and hospitalisation: A potentially deadly combination

Francesco Dentali¹; Mark Crowther²

¹Department of Clinical Medicine, University of Insubria, Varese, Italy; ²Department of Medicine and Pathology and Molecular Medicine, McMaster University and St Joseph's Hospital, Hamilton Ontario, Canada

Venous thromboembolism (VTE) is a common complication of hospitalisation and is associated with morbidity and mortality (1, 2). The annual incidence of VTE increases sharply with age (3). Thus, as the population ages the health burden associated with VTE is expected to grow dramatically. Many studies have identified high-risk groups of surgical and acutely ill medical patients who benefit from antithrombotic prophylaxis (4). Despite this, there seems to be fairly variable and often sub-optimal application of appropriate thromboprophylaxis (5, 6).

Randomised controlled trials (RCTs) and meta-analyses have shown that unfractionated heparin (UFH), low-molecular-weight heparin (LMWH) or fondaparinux reduce symptomatic deep-vein thrombosis (DVT), and symptomatic and fatal pulmonary embolism (PE) in selected medical patients (7). Other studies have found similar results in patients undergoing hip or knee replacement, and cancer surgery (4, 8, 9). As a result of this, evidence-based guidelines recommended the use of antithrombotic prophylaxis in acutely ill high risk medical and surgical patients (4, 10).

Few studies have evaluated the risk of thromboembolic events and the role of

antithrombotic prophylaxis during stays in facilities including convalescent homes and other forms of extended duration skilled-nursing facilities caring for patients who are no longer in the acute phase of an illness but who require a level of care higher than that provided in long-term care institutions.

Although not well studied, a substantial proportion of all VTE events occur in patients in such facilities (11, 12). The reported incidence of symptomatic and ultrasonography detected VTE in post-acute care patients ranges from 5% to 18% (11). In a population-based, nested, case-control study, 13% of all incident VTE cases occurred in residents of post-acute care inpatient facilities (12).

Risk factors for the development of VTE in patients in post-acute care facilities remain largely undefined. Appropriate VTE risk stratification may be especially critical for these patients, many of whom are elderly with multiple co-morbidities and complex medication regimens. These characteristics may increase the risk of both VTE and complications of VTE prophylaxis. Age, previous history of VTE, regional or metastatic-stage cancer, dependence in more than three activities of day living, and pressure ulcers were significantly associated to the occurrence of VTE during hospitalisation in post acute facilities in a previous study (13). Recent studies have shown that development of VTE is associated with an increased mortality in elderly patients and that treatment of VTE is complicated by a not negligible incidence of major bleeding complications in a community setting (14, 15). Unfortunately, despite the frequency of VTE in subacute care facilities, rigorous scientific data providing evidence of the efficacy of prophylaxis in these patients are currently lacking. There is wide hospital-to-hospital variation in the provision of prophylaxis (16) and patients with risk factors for VTE may not receive anti-

thrombotic prophylaxis because of a lack of evidence supporting its efficacy or the fear of bleeding complications.

There is evidence suggesting that VTE prophylaxis may be effective in such patients. Thus, LMWH prophylaxis appeared to reduce the odds of proximal VTE by 40% in unselected older patients with restricted mobility, albeit this result is derived from observational studies (17). Guidelines endorsed by the French Vascular Medicine Society and the French Geriatrics Society (18) recommended pharmacologic prophylaxis for up to six weeks after hip or knee replacement or other major surgical procedure; until discharge in patients with a previous episode of PE or proximal DVT; and for one week or longer, depending on the persistence of the other risk factors such as recent immobility, VTE at other sites, hemiplegia, cancer, acute infectious disease, acute heart failure, acute respiratory failure, and myocardial infarction.

In this issue of *Thrombosis and Haemostasis*, Scannapieco et al. (19) enrolled 3,039 unselected consecutive patients admitted to rehabilitation facilities after medical diseases or surgery. The authors evaluated the frequency of symptomatic objectively confirmed VTE, potential risk factors for VTE, the attitude of physicians towards antithrombotic prophylaxis, and the rate of haemorrhagic complication. The study found that despite a high frequency of use of antithrombotic prophylaxis (about 75% of patients received prophylaxis) patients remained at substantial VTE risk. The rate of major bleeding was low although not negligible. In multivariable analysis the only risk factors significantly associated with the development of VTE were previous VTE and cancer. A surprising obser-

Correspondence to:

Francesco Dentali
Department of Clinical Medicine, University of Insubria
Viale Borri 57, 21100, Varese, Italy
E-mail: fdentali@libero.it
or
Mark Crowther
Department of Medicine and Pathology
and Molecular Medicine
McMaster University and St Joseph's Hospital
50 Charlton Ave East, Hamilton
Ontario, L8N 4A6, Canada
E-mail: crowthrm@mcmaster.ca

Received: August 13, 2010

Accepted: August 13, 2010

Prepublished online: August 30, 2010

doi:10.1160/TH10-08-0527

Thromb Haemost 2010; 104: 655–656

Editorial on ► Scannapieco et al. *Thromb Haemost* 2010; 104: 734–740.

Thrombosis and Haemostasis 104.4/2010

vation in their study was the very high rate of fatal PE. Almost half (48%) of patients with an objective diagnosis of PE died, and PE accounted for all VTE-associated deaths. As the authors point out, this observation may be explained by the low threshold for diagnosing haemodynamically stable PE in such patients. However, this may be also due to the increased case fatality rate of PE in elderly patients attributable to the more frequent presence of co-morbid conditions in this population (15).

In this population, there was a trend toward a higher mortality rate for VTE than for bleeding (2.6% vs. 0.4% of case of death) and the absence of antithrombotic prophylaxis was independently associated with a higher risk of mortality. These results underline the importance of prophylaxis in this setting. However, evidence on the efficacy of antithrombotic prophylaxis in this setting is still lacking and it is not clear which patients may benefit from anti-coagulant therapy.

Given these observations, additional studies are required to prevent VTE in high-risk patients in the post-acute setting. Simple scores identifying patients at high risk of VTE should be derived and validated by prospective randomised controlled trials. Studies must assess the efficacy and safety of different forms and doses of prophylaxis. Importantly, physicians should be aware that PE may develop despite the use of antithrombotic prophylaxis.

References

1. Spyropoulos AC, Hussein M, Lin J, et al. Rates of venous thromboembolism occurrence in medical patients among the insured population. *Thromb Haemost* 2009; 102: 951–957.
2. Fanikos J, Piazza G, Zayaruzny M, et al. Long-term complications of medical patients with hospital-acquired venous thromboembolism. *Thromb Haemost* 2009; 102: 688–693.
3. Silverstein MD, Heit JA, Mohr DN, et al. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. *Arch Intern Med* 1998; 158: 585–593.
4. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; 133: 381S–453S.
5. Kalka C, Spirk D, Siebenrock KA, et al. Lack of extended venous thromboembolism prophylaxis in high-risk patients undergoing major orthopaedic or major cancer surgery. Electronic Assessment of VTE Prophylaxis in High-Risk Surgical Patients at Discharge from Swiss Hospitals (ESSENTIAL). *Thromb Haemost* 2009; 102: 56–61.
6. Goldhaber SZ. Venous thromboembolism prophylaxis: quality, location (hospital vs. home), and duration. *Thromb Haemost* 2009; 102: 1–2.
7. Dentali F, Douketis JD, Gianni M, et al. Meta-analysis: anticoagulant prophylaxis to prevent symptomatic venous thromboembolism in hospitalized medical patients. *Ann Intern Med* 2007; 146: 278–288.
8. Eikelboom JW, Quinlan DJ, Douketis JD. Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials. *Lancet* 2001; 358: 9–15.
9. Bergqvist D, Agnelli G, Cohen AT, et al; ENOXACAN II Investigators. Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. *N Engl J Med* 2002; 346: 975–980.
10. Squizzato A, Ageno W. The 8(th) American College of Chest Physicians Guidelines – a perspective on venous thromboembolism guidelines. *Thromb Haemost* 2009; 101: 31–35.
11. Ambrosetti M, Salerno M, Zambelli M, et al. Deep vein thrombosis among patients entering cardiac rehabilitation after coronary artery bypass surgery. *Chest* 2004; 125: 191–196.
12. Heit JA, O'Fallon WM, Petterson TM, et al. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population-based study. *Arch Intern Med* 2002; 162: 1245–1248.
13. Sellier E, Labarere J, Sevestre MA, et al; Association pour la Promotion de l'Angiologie Hospitalière. Risk factors for deep vein thrombosis in older patients: a multicenter study with systematic compression ultrasonography in postacute care facilities in France. *J Am Geriatr Soc* 2008; 56: 224–230.
14. Spencer FA, Gore JM, Reed G, et al. Venous thromboembolism and bleeding in a community setting. The Worcester Venous Thromboembolism Study. *Thromb Haemost* 2009; 101: 878–885.
15. Vasco B, Villalba JC, Lopez-Jimenez L, et al; RIETE Investigators. Venous thromboembolism in nonagenarians. Findings from the RIETE Registry. *Thromb Haemost* 2009; 101: 1112–1118.
16. Bosson JL, Labarere J, Sevestre MA, et al. Deep vein thrombosis in elderly patients hospitalized in subacute care facilities: a multicenter cross-sectional study of risk factors, prophylaxis, and prevalence. *Arch Intern Med* 2003; 163: 2613–2618.
17. Labarère J, Sevestre MA, Belmin J, et al; Association pour la Promotion de l'Angiologie Hospitalière. Low-molecular-weight heparin prophylaxis of deep vein thrombosis for older patients with restricted mobility: propensity analyses of data from two multicentre, cross-sectional studies. *Drugs Aging* 2009; 26: 263–271.
18. Bosson JL, Labarere J, Barrellier MT, et al; Association for the Promotion of Hospital Angiology. Practice guidelines for the prevention of venous thromboembolism in elderly patients hospitalized in subacute care and rehabilitation facilities. *J Mal Vasc* 2003; 28: 209–218.
19. Scannapieco G, Ageno W, Airolidi A et al. for the TERSICORE Study Group. Incidence and Predictors of Venous Thromboembolism in Post-Acute Care Patients: A Prospective Cohort Study. *Thromb Haemost* 2010; 104: 734–740.