Support Care Cancer (2015) 23:993–999
DOI 10.1007/s00520-014-2448-0

ORIGINAL ARTICLE

Readmission rates due to venous thromboembolism in cancer patients after abdominopelvic surgery, a retrospective chart review

Christine Klimowicz White · Jessica Langholtz · Zackory T. Burns · Susan Kruse · Kimberly Sallee · David H. Henry

Received: 6 March 2014 / Accepted: 14 September 2014 / Published online: 27 September 2014

Abstract
Purpose Venous thromboembolism (VTE) is a known cause of morbidity in the oncology patient population. As hospital readmission rates are more frequently scrutinized, we sought to determine the most common causes of 30-day readmissions in the cancer patient following abdominopelvic surgery. Furthermore, due to the high risk of VTE, there have been guidelines established for prophylaxis. As guidelines are based on asymptomatic VTE, we studied the compliance rates of these guidelines in our institution and the rate of *symptomatic* VTE in the 30-day postoperative period.
Methods We conducted a retrospective chart review at Pennsylvania Hospital of abdominopelvic surgeries between January 1, 2010 and December 31, 2012 in patients with abdominopelvic malignancies, totaling 263 patients.
Results The median age of our patient population was 67 years and 51.3 % were female. The most common malignancy locations were colorectal (44 %) and pancreas (11 %). One patient did not receive perioperative anticoagulation; most received heparin subcutaneously three times daily, mean duration 5.5 days. Fourteen patients (5 %) received outpatient anticoagulation after discharge; only two had a primary intent of VTE prophylaxis. Thirty-five patients (13 %) were readmitted within 30 days of discharge, the most common reasons being abdominal symptoms and postoperative/surgical complications. There was one patient readmitted for a new, symptomatic VTE.
Conclusions Our study showed only one new, symptomatic VTE in the study population, despite 95 % of patients not receiving outpatient anticoagulation, which suggests that continued larger and multicenter trials may be needed to study anticoagulation benefits and risks in this patient population.

Keywords Venous thrombosis · Pulmonary embolism · Hospital readmission · Cancer · Prophylaxis · Heparin

This manuscript in total has not been published elsewhere; however, an abstract presenting this data was accepted and a poster presented at the December 2013 American Society of Hematology (ASH) meeting in New Orleans, Louisiana. The abstract won a 2013 ASH Abstract Achievement Award.

C. K. White (✉) · D. H. Henry
Department of Medicine, Pennsylvania Hospital, 800 Spruce Street, Philadelphia, PA 19107, USA
e-mail: Christine.white@uphs.upenn.edu

S. Kruse · K. Sallee · D. H. Henry
Joan Karnell Cancer Center, Pennsylvania Hospital, 800 Spruce Street, Philadelphia, PA 19107, USA

J. Langholtz
Jefferson Medical College, Thomas Jefferson University, 111 South 11th Street, Philadelphia, PA 19107, USA

Z. T. Burns
Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, UK

Abbreviations

VTE	Venous thromboembolism
ASCO	American Society of Clinical Oncology
UFH	Unfractionated heparin
LMWH	Low-molecular-weight heparin
DVT	Deep venous thrombosis
UPHS	University of Pennsylvania Health System
IRB	Internal review board
BMI	Body mass index
PE	Pulmonary embolism
NOS	Not otherwise specified
g	Grams
dL	Deciliter
L	Liter

mg Milligrams
ACCP American College of Chest Physicians

Introduction

It is established that both oncology patients and patients undergoing major surgery are at an increased risk for venous thromboembolism (VTE). Significantly, VTE is the most common cause of death in oncology patients within the first 30 days postoperatively and a leading cause of death in cancer patients after cancer itself, leading to various recommendations alongside the development of risk stratification models [1, 2]. VTE is not only a serious clinical problem with potentially fatal and extremely costly consequences, but it also is a resource-intensive complication that frequently requires an extended hospitalization stay [3]. In this era of health care reform, it is imperative to understand the incidence of VTE, its strategies for prevention, and its relationship to hospital readmissions in order to ensure patient safety, improve patient outcomes, and minimize hospital costs.

Current guidelines published by the American Society of Clinical Oncology (ASCO) recommend thromboprophylaxis for cancer patients undergoing major surgery for at least 7 to 10 days postoperatively with either unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH). Prophylaxis should be extended for up to 4 weeks postoperatively for those cancer patients undergoing major abdominal or pelvic surgery with high-risk features, such as restricted mobility, obesity, history of VTE, or metastatic disease [4]. These guidelines are based on several studies that utilized bilateral lower extremity screening venography to detect both symptomatic and asymptomatic VTE [5]. It has been previously shown that extended thromboprophylaxis is associated with a significantly lower risk of asymptomatic deep venous thrombosis (DVT), but there is, unfortunately, limited data assessing this recommendation in the setting of symptomatic DVT [6].

Thus, this study focuses on VTE in the oncology patient population, in the postoperative setting. We investigated the most frequent causes of readmission of oncology patients after abdominal or pelvic surgery, specifically examining the incidence of *symptomatic* VTE. Due to the high mortality rate of VTE in oncology patients, we sought to determine whether the current guidelines for VTE were being followed, and subsequently, if the benefits of extended anticoagulation outweighed potential harms in this patient population.

Materials and methods

The University of Pennsylvania Health System (UPHS) Internal Review Board (IRB) approved a retrospective chart review for abdominal and pelvic surgeries performed at Pennsylvania Hospital from January 1, 2010 to December 31, 2012.

Using the outpatient surgical billing systems of Ambulatory practice management (APM, by Epic) and IDX (by General Electric), we identified 6949 patients in the Division of Gastrointestinal Surgery at Pennsylvania Hospital who underwent abdominal or pelvic surgery in the time frame specified. We used the diagnosis code to include only those patients with an abdominal or pelvic malignancy or neoplasm. Patients were excluded from the study if they did not have a proven abdominal or pelvic malignancy, or if the surgery was an outpatient procedure. There were 267 patients who qualified for more detailed data collection. Four patients died during hospitalization and were excluded as they did not have potential for readmission, bringing the final study population to 263.

Data was collected using the UPHS electronic medical record systems, Medview and Epic, and included patient demographics of sex, age, and body mass index (BMI); type and site of malignancy and presence and location of metastatic disease; type of surgery; any use of anticoagulation in the perioperative period, including reason for use and timing; lab data specifically hemoglobin, leukocyte count, platelet count, and creatinine available closest to discharge date; and any hospital readmission within 30 days of discharge, noting the number of days to readmission, cause of readmission, and presence of symptomatic VTE. VTE was defined as DVT and/or pulmonary embolism (PE). Both inpatient and outpatient records were reviewed postoperatively to account for any readmissions that occurred in or less than 30 days documented in the UPHS health system or in another institution. If there was no UPHS inpatient record and/or the postoperative clinic visit note with the surgeon did not document an admission to any hospital, it was presumed that there was no readmission. If the patient was lost to follow-up after the surgery, it was recorded as such, and was not considered as a readmission or non-readmission.

The primary study outcome was to define the most common causes of 30-day postoperative readmissions in oncology patients. Secondary outcomes were to determine if VTE prophylaxis was prescribed for this patient population upon discharge, to assess compliance with VTE guidelines, and to determine if VTE prophylaxis resulted in reduced 30-day postoperative readmissions for VTE.

Results

The median age of our patient population was 67 years (range 23–92) with 51.3 % of the patients being female and 48.7 % were male. Median BMI was 25.4 (range 13.4–60.1). The most common malignancy locations were colorectal (44 %), pancreas (11 %), gastroesophageal junction (6 %), and retroperitoneum (6 %). The most common types of

malignancies were adenocarcinoma (61 %) and carcinoma not otherwise specified (NOS) (16 %); 42 % had metastatic disease, most commonly in the liver (14 %) and lymph nodes (14 %) (Table 1).

Lab results were collected upon discharge: median hemoglobin level was 9.9 g/dL, median leukocyte count was 7.8×10^9/L, median platelet count was 233×10^9/L, and median creatinine was 0.86 mg/dL.

Only one patient did not receive inpatient perioperative anticoagulation; 243 patients (92 %) received anticoagulation with heparin 5000 units subcutaneously, three times daily. The median duration of inpatient perioperative anticoagulation was 5.5 days (range 1–38). Several patients had a change in their anticoagulation regimen during hospitalization or received dual anticoagulation therapy (Table 2).

Thirteen patients (5 %) received outpatient anticoagulation which included LMWH (3 patients) and/or warfarin (10 patients), with three patients receiving this as a new medication. Only two of these patients received anticoagulation with the primary reason identified as VTE prevention. Other reasons for discharge on anticoagulation included known VTE and cardiovascular disease. In addition, 41 patients (16 %) were discharged on aspirin 81 mg daily, 12 patients (5 %) on aspirin 325 mg daily, 2 patients (1 %) on aspirin of unknown dosage, and 10 patients (4 %) on clopidogrel 75 mg daily. Several patients were discharged on various combinations of anticoagulants (Table 3).

Within 30 days of discharge, 35 patients (13 %) were readmitted to a hospital at a median of 7 days post-discharge (range 1–30). Fourteen patients (5 %) were lost to follow-up. Patient characteristics were similar between those readmitted within 30 days post-discharge and those not readmitted (Table 4).

The most common reasons for readmission were abdominal symptoms (11), postoperative complications and surgical problems (11), infectious causes (8), cardiopulmonary symptoms (6), and electrolyte disturbances (2). Three patients were readmitted with multiple presenting symptoms, and two patients had planned readmissions for a subsequent surgical procedure.

Two patients were readmitted with a symptomatic VTE. One of these patients had a known VTE that was diagnosed and treated prior to readmission, and thus was excluded from final assessment. The remaining patient, who had colorectal adenocarcinoma, was readmitted 4 days post-discharge for chest pain and was later diagnosed with a symptomatic PE. This patient notably did receive VTE prophylaxis during admission.

Table 1 Baseline patient and disease characteristics and lab values

Characteristics	No. of patients	Percent	Values
Age, year			
Median			67
Range			23–92
Gender			
Male	128	48.7	
Female	135	51.3	
BMI			
Median			25.4
Range			13.4–60.1
Malignancy location			
Colorectal	115	43.7	
Pancreas	28	10.6	
Gastroesophageal junction	17	6.4	
Retroperitoneum	16	6.1	
Other	87	33.1	
Malignancy type			
Adenocarcinoma	162	61.6	
Carcinoma	42	16.0	
Other	59	22.4	
Metastatic disease	111	42.2	
Liver	38	34.2	
Lymph nodes	36	32.4	
Other	37	33.3	
Hemoglobin (g/dL)			
Median			9.9
Range			6.6–14.9
Leukocyte count (10^9 L)			
Median			7.8
Range			1.4–22.4
Platelet count (10^9 L)			
Median			233
Range			77–871
Creatinine (mg/dL)			
Median			0.86
Range			0.07–9.43

Table 2 Type and duration of inpatient perioperative anticoagulation

	No. of patients	Percent	Values
Type of anticoagulation			
Heparin subcutaneous (prophylaxis)	257	98	
Heparin infusion	3	1.1	
Dalteparin subcutaneous (prophylaxis)	8	3.0	
Coumadin	10	3.8	
Not applicable	1	0.4	
Duration of anticoagulation (days)			
Median			5.5
Range			1–38

Table 3 Types of outpatient perioperative anticoagulation

	Total patients (n=263)	Patients readmitted (n=35)	Patients not readmitted (n=214)
Warfarin	10	2	8
Dalteparin	2	0	2
Aspirin	55	7	46
Clopidogrel	10	2	6
Not applicable	203	28	165

Discussion

Hospital readmissions are, unfortunately, common and costly; it is estimated that one out of four hospitalized patients will be readmitted, increasing the financial burden of already increasing health care costs [7]. Readmission rates are rising and are likely to become quality indicators of a surgeon's performance, potentially alongside other quality control markers, such as decreased length of hospital stay and patient comorbidities [8, 9]. In a previous study, 19 % of patients were readmitted, following a pancreaticoduodenectomy, with the

Table 4 Comparison of characteristics in patients readmitted and not readmitted within 30 days

	Patients readmitted (n=35)			Patients not readmitted (n=214)		
Characteristics	No. of patients	Percent	Values	No. of patients	Percent	Values
Age, year						
Median			66			67
Range			38–89			30–92
Gender						
Male	18	51.4		101	47.0	
Female	17	48.6		114	53.0	
BMI						
Median			25.8			25.4
Range			15.4–39.8			13.4–60.1
Malignancy location						
Colorectal	12	3.2		95	44.4	
Pancreas	7	20.0		19	8.9	
Gastroesophageal junction	1	2.9		16	7.4	
Retroperitoneum	2	5.7		14	6.5	
Other	13	37.1		70	32.7	
Malignancy type						
Adenocarcinoma	21	60.0		131	61.2	
Carcinoma	9	25.7		31	14.5	
Other	5	14.3		52	24.3	
Metastatic disease	15	42.9		88	41.1	
Liver	3	8.6		31	14.4	
Lymph nodes	6	17.1		29	13.5	
Other	6	17.1		28	13.0	
Hemoglobin (g/dL)						
Median			10.1			9.8
Range			6.6–13.9			7.3–14.9
Leukocyte count (10^9 L)						
Median			7.8			7.8
Range			1.4–16.3			2.7–22.4
Platelet count (10^9 L)						
Median			244			232
Range			92–653			77–871
Creatinine (mg/dL)						
Median			0.73			0.73
Range			0.34–1.63			0.07–6.46

most common reasons, including nausea, vomiting, infection, and abdominal pain [10]. Similarly, we found that 13 % of our study patients were readmitted to a hospital within 30 days, most commonly for abdominal symptoms or postoperative complications.

Current guidelines by both ASCO and the American College of Chest Physicians (ACCP) recommend extended 4-week thromboprophylaxis in high-risk postoperative oncology patients undergoing major abdominal and pelvic surgery [4, 11]. Previous studies have reported a median time to diagnose VTE of 9 to 15 days and a mean time of 8.6 days, which is comfortably within the 30-day window of our study [12–14]. Only 5 % of patients in our study were discharged from the hospital on anticoagulation. Although this constitutes guideline noncompliance, there was only one readmission due to a *symptomatic* VTE, indicating that the incidence of symptomatic VTE in this population may not be as high as previously suggested.

Although guidelines are solely recommendations, they are developed to aid in the best management of clinical conditions with a goal to yield the best patient outcomes. They are developed around clinical data and trials or based on expert opinion to steer clinicians in making best decisions for patient care. The ASCO guidelines recommending extended thromboprophylaxis are based on four studies that analyzed the incidence of both symptomatic and asymptomatic VTE in a similar patient population using mandatory bilateral venography, which is no longer routinely used in the clinical setting [4]. Multiple studies have reported an association between asymptomatic DVT and the development of symptomatic VTE, but there is not yet clear evidence proving a benefit to the patient in reducing asymptomatic VTE [15]. Venography is an antiquated and invasive procedure, and it is possible that the procedure itself may not have the benefit to justify the risk. A review published by the Cochrane Collaboration was used to support the ASCO guidelines and found that, although the rate of asymptomatic VTE was significantly decreased with extended thromboprophylaxis, there was no significant difference in the rate of mortality or PE between patients who received in-hospital prophylaxis and patients who received extended prophylaxis [5].

Given the low incidence of symptomatic VTE in our patient population, we sought to determine whether extended thromboprophylaxis might instead cause more potential harm rather than benefit. A 2008 review by Akl et al. predicted that the incidence of major bleeding in a high-risk population is 59 per 1000 for cancer patients receiving extended duration thromboprophylaxis, compared to 20 per 1000 for those receiving thromboprophylaxis only during their hospital stay. The study also expected minor bleeding for 79 per 1000 of high-risk patients receiving extended thromboprophylaxis, compared to 60 per 1000 of high-risk patients receiving limited thromboprophylaxis [6]. Although these results are not statistically significant, they are still clinically significant as extended thromboprophylaxis may lead to an increased incidence of side effects in patients who have a low risk of developing VTE.

As the rate of symptomatic VTE was surprisingly low, and bleeding while on anticoagulation remains a serious side effect, we attempted to apply the Khorana model to our study population, which serves as a predictive model for chemotherapy-associated VTE by calculating patient risk level for thrombosis when considering several validated parameters prior to chemotherapy [16]. Based on this model, no high-risk patients developed VTE, and in fact the patient in our study readmitted with VTE was considered an intermediate risk. Nevertheless, this model was applied to postoperative patients and not to pre-chemotherapy patients, thus violating the model assumptions and cannot be validated with the data gathered in this study. Due to the limitations of the Khorana model in this population, we suggest that a new model be created to predict VTE risk in postoperative cancer patients.

In this study, we showed that 64 patients (24 %) were discharged on aspirin and/or clopidogrel, drugs which are considered minor anticoagulants. Many of these patients had been previously taking these medications prior to hospitalization, and none of these patients developed VTE. It is possible that the use of aspirin and/or clopidogrel played a role in VTE prevention and, consequently, this study's low incidence of symptomatic VTE. The use of aspirin as an anticoagulant for perioperative VTE prophylaxis is currently being debated. The ACCP does not recommend aspirin alone for perioperative VTE prophylaxis in any patient group; however, the American Academy of Orthopedic Surgeons now suggests that aspirin may be effective as a method of orthopedic postoperative VTE prophylaxis [17]. While aspirin is inexpensive, seemingly cost-effective, and does not require monitoring or injections compared to other forms of anticoagulation, there is no significant evidence supporting its use in VTE prophylaxis in this patient population [18]. The Pulmonary Embolism Prevention Trial randomized over 17,000 patients to receive aspirin 160 mg daily or placebo for 35 days perioperatively for hip fracture or elective hip or knee arthroplasty. Aspirin was found to reduce the risk of symptomatic VTE by 36 % and fatal PE by 53 %; however, it was associated with an increase in minor gastrointestinal bleeding, which demonstrates the need to weigh its benefits against potential harm [19]. A recent multi-center trial showed that extended prophylaxis with aspirin was not inferior to dalteparin after total hip arthroplasty [20]. Clopidogrel, although not as widely studied as aspirin in this setting, may also lead to decreased risk of thrombosis; however, this too must be weighed against the risk of hemorrhage. While patients with oncologic diagnoses have a baseline hypercoagulable state and thus have different pathology and physiology than those patients without a malignancy undergoing orthopedic procedures, it may still be possible to incorporate and apply this data to cancer patients in further trials.

This study has several limitations. By the nature of our retrospective chart review, there is possibility of selection bias as only patients who had documented encounters in the UPHS system were included in the 30-day follow-up. Fourteen patients (5 %) were lost to follow-up. It is unknown if some of those patients may have developed symptomatic VTE within 30 days and presented to another facility without later returning to UPHS. This was a small study of 263 patients, so it is possible that our sample size was not large enough to detect more VTE to corroborate the current guidelines. A larger sample size would be needed to prove or disprove any guideline; however, this data is the first reported that provides no evidence supporting the recommendations, and thus, larger and more studies are needed to confirm or reject our findings. The 30-day time period used in this analysis may have excluded PE and DVT that were diagnosed after the time restriction. As this study was a retrospective chart review, patients were not screened for asymptomatic VTE, and this may have led to results different from those on which recommendations are based. Finally, surveillance bias may have influenced the screening and detection of VTE in the study population, as it has been repeatedly shown that the use of imaging studies to assist with VTE detection is not well standardized among clinicians and institutions. Due to the retrospective nature of this study, we are unable to adequately assess if detection of VTE was standardized across all of the clinicians involved in our study [21].

Although it is agreed that VTE is an important cause of morbidity and hospital cost, there is still much debate about the appropriate prophylactic treatment for VTE. We recommend for the need for extended thromboprophylaxis to be reassessed due to the low incidence of readmission from symptomatic VTE in the postoperative population of those with abdominal or pelvic malignancies. Further multicenter studies will need to be conducted to better quantify the need for VTE prophylaxis, identify high-risk populations, and determine if risk of anticoagulation outweighs benefit as we strive to care for our oncology patients in a changing health care environment.

Conflict of interest Authors declare no conflicts of interest.

References

1. Agnelli G, Bolis G, Capussotti L, Scarpa RM, Tonelli F, Bonizzoni E, Moia M, Parazzini F, Rossi R, Sonaglia F, Valarani B, Bianchini C, Gussoni G (2006) A clinical outcome-based prospective study on venous thromboembolism after cancer surgery: the @RISTOS project. Ann Surg 243:89–95
2. Khorana AA (2012) Cancer-associated thrombosis: updates and controversies. In: Burns LJ (ed) Hematology Am Soc Hematol Educ Program 2012. American Society of Hematology, Rochester, pp 626–630
3. Elting LS, Escalante CP, Cooksley C, Avritscher EB, Kurtin D, Hamblin L, Khosla SG, Rivera E (2004) Outcomes and cost of deep vein thrombosis among patients with cancer. Arch Intern Med 164: 1653–1661
4. Lyman GH, Khorana AA, Kuderer NM, Lee AY, Arcelus JI, Balaban EP, Clarke JM, Flowers CR, Francis CW, Gates LE, Kakkar AK, Key NS, Levine MN, Liebman HA, Tempero MA, Wong SL, Prestrud AA, Falanga A (2013) Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 31:2189–2204
5. Rasmussen MS, Jorgensen LN, Wille-Jorgenson P (2009) Prolonged thromboprophylaxis with low molecular weight heparin for abdominal or pelvic surgery. Cochrane Database Syst Rev 1, CD004318
6. Akl EA, Terrenato I, Barba M, Sperati F, Muti P, Schunemann HJ (2008) Extended perioperative thromboprophylaxis in patients with cancer: a systematic review. Thromb Haemost 100:1176–1180
7. Stefan MS, Pekow PS, Nsa W, Priya A, Miller LE, Bratzler DW, Rothberg MB, Goldberg RJ, Baus K, Lindenauer PK (2013) Hospital performance measures and 30-day readmission rates. J Gen Intern Med 28:377–385
8. Schneider EB, Hyder O, Brooke BS, Efron J, Cameron JL, Edil BH, Schulick RD, Choti MA, Wolfgang CL, Pawlik TM (2012) Patient readmission and mortality after colorectal surgery for colon cancer: impact of length of stay relative to other clinical factors. J Am Coll Surg 214:390–398
9. Martin RC, Brown R, Puffer L, Block S, Callender G, Quillo A, Scoggins CR, McMasters KM (2011) Readmission rates after abdominal surgery: the role of surgeon, primary caregiver, home health, and subacute rehab. Ann Surg 254:591–597
10. Rosemurgy AS, Luberice K, Paul H, Co F, Vice M, Toomey P, Choung E, Ross SB (2012) Readmissions after pancreaticoduodenectomy: efforts need to focus on patient expectations and nonhospital medical care. Am Surg 78:837–843
11. Gould MK, Garcia DA, Wren SM, Karanicolas PJ, Arcelus JI, Heit JA, Samama CM (2012) Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 141:e227S–277S
12. Davenport DL, Vargas HD, Kasten MW, Xenos ES (2012) Timing and perioperative risk factors for in-hospital and post-discharge venous thromboembolism after colorectal cancer resection. Clin Appl Thromb Hemost 18:569–575
13. Toledano TH, Kondal D, Kahn SR, Tagalakis V (2013) The occurrence of venous thromboembolism in cancer patients following major surgery. Thromb Res 131:e1–e5
14. Smith BR, Diniz S, Stamos M, Nguyen NT (2011) Deep venous thrombosis after general surgical operations at a university hospital: two-year data from the ACS NSQIP. Arch Surg 146:1424–1427
15. Varpe P, Huhtinen H, Rantala A, Gronross J (2009) Thromboprophylaxis following surgery for colorectal cancer – is it worthwhile after hospital discharge? Scand J Surg 98:58–61
16. Khorana AA, Kuderer NM, Culakova E, Lyman GH, Francis CW (2008) Development and validation of a predictive model for chemotherapy-associated thrombosis. Blood 111:4902–4907
17. Michota FA (2009) Prevention of venous thromboembolism after surgery. Cleve Clin J Med 76:S45–S52
18. Bradley CT, Brasel KJ, Miller JJ, Pappas SG (2010) Cost-effectiveness of prolonged thromboprophylaxis after cancer surgery. Ann Surg Oncol 17:31–39
19. Pulmonary Embolism Prevention (PEP) Trial Collaborative Group (2000) Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet 355:1295–1302

20. Anderson DR, Dunbar MJ, Bohm ER, Belzile E, Kahn SR, Zukor D, Fisher W, Gofton W, Gross P, Pelet S, Crowther M, MacDonald S, Kim P, Pleasance S, Davis N, Andreou P, Wells P, Kovacs M, Rodger MA, Ramsay T et al (2013) Aspirin versus low-molecular-weight heparin for extended venous thromboembolism prophylaxis after total hip arthroplasty: a randomized trial. Ann Intern Med 158:800–806
21. Bilimoria KY, Chung J, Ju MH, Haut ER, Bentrem DJ, Ko CY, Baker DW (2013) Evaluation of surveillance bias and the validity of the venous thromboembolism quality measure. JAMA 310:1482–1489