The American Society of Colon and Rectal Surgeons Clinical Practice Guideline for the Prevention of Venous Thromboembolic Disease in Colorectal Surgery

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Prepared by the Clinical Practice Guidelines Committee of The American Society of Colon and Rectal Surgeons

The American Society of Colon and Rectal Surgeons is dedicated to ensuring high-quality patient care by advancing the science, prevention, and management of disorders and diseases of the colon, rectum, and anus. The Clinical Practice Guidelines Committee is composed of society members who are chosen because they have demonstrated expertise in the specialty of colon and rectal surgery. This committee was created to lead international efforts in defining quality care for conditions related to the colon, rectum, and anus. This is accompanied by development of clinical practice guidelines based on the best available evidence. These guidelines are inclusive but not prescriptive. Their purpose is to provide information to support decision making, rather than to dictate a specific form of treatment. These guidelines are intended for the use of all practitioners, health care workers, and patients who desire information about the management of the conditions addressed by the topics covered in these guidelines. It should be recognized that the guidelines should not be deemed inclusive of all proper methods of care nor exclusive of methods of care reasonably directed toward obtaining the same results. The ultimate judgment regarding the propriety of any specific procedure must be made by the physician in light of all the circumstances presented by the individual patient.

STATEMENT OF THE PROBLEM

Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), is a serious health problem in the United States, with an estimated 600,000 to 900,000 cases occurring annually. Venous thromboembolism is a common and often morbid complication of any major surgery. Historical estimates from the control groups of randomized prophylaxis trials showed that over 30% of patients undergoing colorectal surgery developed DVT compared with 20% for all patients undergoing general surgery. Although VTE may occur after any surgical procedure, patients undergoing colorectal surgery are at significant risk for this perioperative complication with rates as high as 9% even in patients receiving VTE chemoprophylaxis. This elevated risk of a thrombotic complication is associated with intraoperative patient positioning, pelvic dissection, and the presence of additional risk factors common in this patient cohort, including preexisting inflammation in the form of malignancy or IBD. Although the focus of VTE prevention is often on those with malignancy, patients with IBD have a 2- to 3-fold increased risk of DVT and PE compared with the general population. Results from a multicenter randomized controlled trial in patients undergoing colorectal surgery comparing pharmacological prophylaxis methods using ultrasound and venography for diagnosis showed the rate of proximal DVT, defined as popliteal or more proximal veins, to be 2.6% to 2.8%. Population-based studies have also tried to estimate the risk of DVT after colorectal surgery, although the lack of a
ulceration that can result in substantial disability.10,11

Postoperative VTE remains a significant health care issue with both short- and long-term morbidity for the individual patient and significant costs for the health care system. The aim of this clinical practice guideline is to present and grade the evidence base for preoperative risk assessment and thromboprophylaxis in patients undergoing colorectal surgery.

METHODOLOGY

This clinical practice guideline expands on the previous Practice Parameters for the Prevention of Venous Thrombosis published by the American Society of Colon and Rectal Surgeons (ASCRS) in 2006.12 A clinical practice guideline addressing specific issues pertaining to ambulatory colorectal surgery has been recently published that also outlines evidence specifically pertaining to thromboprophylaxis for ambulatory colorectal surgery.13 The majority of articles used to construct the prior guideline were dated in 2002 and earlier; as such, an organized search of MEDLINE, PubMed, and the Cochrane Database of Systematic Reviews was performed of articles from January 2003 through December 2016.12 See Appendix 1 (http://links.lww.com/DCR/A488) for the research strategy used for MEDLINE and PubMed; 1904 titles were screened, and 312 references were directly reviewed, ultimately yielding 79 references for consideration. A similar but colorectal and pelvic surgery-targeted search was performed, yielding an additional 19 unique references. In addition, the Cochrane Database of Systematic Reviews was searched for deep venous thrombosis, resulting in 65 titles, which were again screened and yielded 5 references for inclusion. Prospective, randomized controlled trials and meta-analyses were given preference in developing these guidelines. Directed searches of the embedded references from the primary articles were also performed in certain circumstances. Members of the ASCRS practice guidelines committee worked in joint production of these guidelines from inception to final publication. The final source material used was evaluated for the methodological quality, the evidence base was examined, and a treatment guideline was formulated by the subcommittee for this guideline. When agreement was incomplete regarding the evidence base or treatment guideline, consensus from the committee chair, vice chair, and 2 assigned reviewers determined the outcome. The final grade of recommendation was performed using the Grade of Recommendation, Assessment, Development, and Evaluation (GRADE) system (Table 1).14 Members of the ASCRS practice guidelines committee worked in joint production of these guidelines from inception to final publication. Recommendations formulated by the subcommittee were reviewed by the entire Clinical Practice Guidelines Committee. Final recommendations were approved by the ASCRS Clinical Guidelines Committee and ASCRS Executive Committee. In general, each ASCRS Clinical Practice Guideline is updated every 5 years.

MANAGEMENT RECOMMENDATIONS

1. The use of a VTE risk assessment model is recommended to guide VTE prophylaxis in patients undergoing colorectal surgery. Grade of Recommendation: Weak recommendation based on high-quality evidence, 2A.

Patient-specific risk factors for VTE, bleeding risks, and the specific surgical procedure must all be considered to balance the risks and benefits of specific methods of thromboprophylaxis. Risk factors for VTE are numerous, and unfortunately most hospitalized patients will have at least 1 risk factor for VTE, and as many as 40% will carry 3 or more risk factors.15 Therefore, determining the appropriate patients to receive extended thromboprophylaxis based on risk factors alone often is problematic. In addition, the specific quantifiable risk imparted by various conditions alone or in conjunction may vary. Factors may be patient, disease, or surgery specific and may or may not be modifiable or transient (Table 2). Various methodologies attempt to quantify the risk of developing VTE.

Recent Antithrombotic Therapy and Prevention of Thrombosis, 9th edition guidelines1 for prevention of VTE in nonorthopedic surgical patients describe stratification of VTE risk in patients undergoing general and abdomino-pelvic surgery among others. Two risk assessment models are described yielding very-low-risk, low- to moderate-risk, and high-risk groups (Table 3). First, the Rogers score is based on a model from a study of over 183,000 patients and it assigns points based on variables found to be independent predictors of VTE risk, including type of operation, work-relative value units, patient characteristics, and laboratory values.16 Second, the Caprini score, which is easier to use, is based on various VTE risk factors and has been validated in a retrospective analysis.17–19 Adult colorectal surgical patients undergoing abdominopelvic surgery are most commonly in the highest-risk subgroup, by nature of their...
age, surgical indication, and necessary surgery, with an associated 6% risk of developing a perioperative symptomatic VTE. The importance of including some form of risk assessment in decision making is demonstrated by numerous VTE prophylaxis implementation studies that have incorporated risk assessment into clinical decision tools.20,21 In summary, an individualized assessment of the risk of thrombosis and bleeding is recommended in patients undergoing colorectal surgery to allow the implementation of an appropriate VTE prophylaxis regimen and to help minimize the morbidity and mortality of VTEs.

2. Mechanical strategies for VTE prophylaxis, including early mobilization and intermittent pneumatic compression (IPC) devices, should be deployed for patients undergoing colorectal surgery. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.

Methods of mechanical VTE prophylaxis include elastic stockings (ES), IPC devices, and early mobilization. These methods address the venous stasis portion of the Virchow triad by increasing venous blood flow and have associated benefits and limitations. Systematic reviews evaluating the efficacy of ES compared with no prophylaxis have demonstrated up to a 65% decrease in the incidence of all DVT among surgical patients.22,23 These studies, however, failed to confirm or exclude a reduction in proximal DVT or PE with the use of ES. Studies examining the effectiveness of ES in nonsurgical populations have shown mixed results. A large multicenter randomized control trial of patients with acute stroke failed to identify or exclude a reduction in fatal or nonfatal PE or proximal or symptomatic DVT when comparing thigh-length ES and routine care with routine care alone. Furthermore, the use of ES was associated with a 4-fold increase in skin complications, such as skin breaks or blisters.24 Addition of ES to pharmacological prophylaxis has shown a 60% reduction in DVT, including asymptomatic and distal DVT, and a 72% reduction in proximal DVT, but a difference in the risk of PE was neither confirmed nor excluded.7

Intermittent pneumatic compression devices decrease venous stasis and promote fibrinolysis. Compared with no prophylaxis, IPC use is associated with an ~50% reduction in symptomatic and proximal DVT, but results did not demonstrate or exclude an effect on PE.25 In pooled results from various studies, the addition of IPC to chemical VTE prophylaxis (primarily low-dose unfractionated heparin (LDUH) and low-molecular-weight heparin (LMWH)) was associated with a possible reduction in symptomatic and asymptomatic DVT (OR, 0.45), but differences in proximal

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**TABLE 1. The GRADE system: grading recommendations**

<table>
<thead>
<tr>
<th>Description</th>
<th>Benefit vs risk and burdens</th>
<th>Methodological quality of supporting evidence</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>Strong recommendation, High-quality evidence</td>
<td>Benefits clearly outweigh risk and burdens or vice versa</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
</tr>
<tr>
<td>1B</td>
<td>Strong recommendation, Moderate-quality evidence</td>
<td>Benefits clearly outweigh risk and burdens or vice versa</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
</tr>
<tr>
<td>1C</td>
<td>Strong recommendation, Low-or very-low-quality evidence</td>
<td>Benefits clearly outweigh risk and burdens or vice versa</td>
<td>Observational studies or case series</td>
</tr>
<tr>
<td>2A</td>
<td>Weak recommendation, High-quality evidence</td>
<td>Benefits closely balanced with risks and burdens</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
</tr>
<tr>
<td>2B</td>
<td>Weak recommendations, Moderate quality evidence</td>
<td>Benefits closely balanced with risks and burdens</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
</tr>
<tr>
<td>2C</td>
<td>Weak recommendation, Low-or very-low-quality evidence</td>
<td>Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced</td>
<td>Observational studies or case series</td>
</tr>
</tbody>
</table>

GRADE = Grades of Recommendation, Assessment, Development, and Evaluation; RCT = randomized controlled trial.
DVT or PE were neither confirmed or excluded. A 2008 Cochrane review found that, when compared with IPC alone, combined prophylaxis modalities (defined as IPC and pharmacological prophylaxis) significantly decreased the incidence of VTE. Furthermore, when compared with pharmacological prophylaxis alone, combined modalities significantly reduced the incidence of DVT, but the effect on PE is unknown. Overall, either ES or IPC devices should be used, although the data supporting IPC device, especially in combination with chemoprophylaxis, are stronger.

Early mobilization and ambulation as a strategy to prevent VTE is founded on the fact that immobilized patients are at high risk for VTE. Yet, there is a lack of high-quality evidence looking specifically at early mobilization or early ambulation to prove a VTE reduction benefit. A recent study implemented a care program emphasizing early postoperative mobilization through a standardized mobilization order for patients to be “out of bed” at least 3 times daily beginning on the day of surgery, along with mandatory VTE risk stratification. The study found that risk-adjusted VTE outcomes declined from a preimplementation OR of 3.41 to a postimplementation OR of 0.94. Nevertheless, VTE prevention guidelines stress early mobilization as a fundamental component of VTE prophylaxis in all patients. Early mobilization should be encouraged for all patients in addition to the use of IPC devices.

3. Pharmacological thromboprophylaxis with either LMWH or LDUH should typically be given to patients undergoing colorectal operations who are deemed to be at moderate or high risk for VTE, who are not identified as high risk for bleeding complications. Grade of Recommendation: Strong recommendation based on high-quality evidence, IA.

Pharmacological prophylaxis is typically administered as LDUH or LMWH. In a review of more than 70 randomized controlled trials of LDUH (>16,000 patients) in several surgical subspecialties including general surgery, LDUH therapy was associated with a reduction in the incidence of screened DVT from 22% to 9% and a 47% reduction in the incidence of PE. However, LDUH was also associated with a 57% increase in the odds of nonfatal major bleeding. A meta-analysis comparing LMWH with no prophylaxis or placebo and unfractionated heparin in general surgery found that LMWH reduced the risk of clinical VTE by 70%, but was associated with an increased risk of wound hematoma (relative risk, 1.88; 95% CI, 1.54–2.28). The Canadian Colorectal DVT Trial, which included 936 patients, confirmed that LMWH (enoxaparin 40 mg daily) is as effective and safe as LDUH (5000 units every 8 hours) in VTE prevention after colorectal surgery. The incidence of screened VTE on venography was 9.4% in both groups, whereas the rate of proximal DVT was 2.6% in the LDUH group and 2.8% in the LMWH group. A Cochrane review pooled data from 11 studies in patients undergoing colorectal surgery to compare the efficacy of LDUH and LMWH and found that each was significantly more effective than placebo or no treatment in VTE prevention (OR, 0.32; CI, 0.20–0.53). In the 4 studies that directly compared LDUH and LMWH, the 2 treatments were equally effective (OR, 1.01; 95% CI, 0.69–1.52).

An area of concern for all surgeons is the potential risk of bleeding associated with VTE chemoprophylaxis. McLeod et al reported significantly more overall bleeding events in patients receiving LMWH compared with those receiving LDUH. The minor bleeding event rate was significantly increased, although the difference in the rate of major bleeding events was not significant. A similar trend was observed in the ENOXACAN study: major bleeding was seen in 4.1% of patients receiving LMWH and 2.9% of those receiving LDUH. However, a more recent meta-analysis did not observe increased bleeding with LMWH in patients undergoing general surgery.

4. For high VTE risk patients undergoing colorectal surgery, where chemoprophylaxis is contraindicated or previously found to be insufficient, an inferior vena cava (IVC) filter may be considered. Grade of
Recommendation: Weak recommendation based on low-quality evidence, 2C.

There is a marked paucity of data examining the use of IVC filters in elective colorectal surgery. In the trauma literature, a meta-analysis reported significantly lower pooled odds of PE (OR, 0.21; CI, 0.09–0.49) in patients who had an IVC filter placed compared with matched historical controls. However, the analysis concludes that, given the lack of contemporary use of chemoprophylaxis across studies, no safe conclusions can be made. The PREPIC trial was an open randomized controlled trial of 400 participants identified as high risk for PE with documented proximal DVT with or without PE who received standard anticoagulation with or without an IVC filter. At 8 years, IVC filters reduced the risk of PE but increased the risk of DVT and had no effect on survival. As such, patients with contraindications to chemoprophylaxis, or patients who have incurred a VTE in the setting of chemoprophylaxis that face significant risk of PE with upcoming colorectal surgery, may benefit from an IVC filter discussion with multidisciplinary assessment. Finally, if needed, a corresponding filter retrieval plan may be instituted and follow-up to avoid unwarranted complications from a long-dwelling filter.

5. In patients undergoing colorectal cancer resection deemed to be at high risk for VTE, strong consideration should be given to extended-duration pharmacological thromboprophylaxis (4 weeks). Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.

Increasing utilization of minimally invasive surgery and enhanced recovery programs with increasing scrutiny over resource utilization has reduced the average in-hospital length of stay after colorectal resection. Thus, many patients are discharged before postoperative day 7, but most of the guidelines on the length of in-patient thromboprophylaxis are derived from data based on thromboprophylaxis for at least 7 days postoperatively. Although the risk of VTE is highest in the first 2 weeks postoperatively, VTE risk remains elevated for several weeks after surgery. Agnelli et al reported a prospective observational study of 2373 patients who underwent oncological surgery, where only clinically overt VTE events were recorded. Venous thromboembolism was the commonest cause of postoperative mortality with 40% of events occurring more than 21 days postoperatively. An analysis of colorectal resections captured in the National Surgical Quality Improvement Program found a postdischarge VTE rate of 0.67%. Obesity, preoperative steroid use, high ASA class, and predischarge complications were all independently associated with subsequent postdischarge VTE. A recent article from the Washington State Surgical Care and Outcome Assessment program (SCOAP) analyzed the incidence of thromboembolic complications and contemporary VTE prophylaxis following colorectal surgery. Among 16,120 patients, the 90-day VTE rate was 2.2%, with 39% of VTE events occurring following the index discharge.

A number of randomized controlled trials (RCTs) have addressed the use of extended-duration thromboprophylaxis (typically LMWH) for a period of 28 days following surgery compared with a shorter in-patient-based protocol (typically 7–10 days). A Cochrane review of these RCTs found that the incidence of screened VTE after open abdominal or pelvic surgery was 14.3% in the control group compared with 6.1% in the extended duration thromboprophylaxis group (OR, 0.41; 95% CI, 0.26–0.63). The number needed to treat to avoid 1 case of VTE was 13, whereas the number needed to treat to avoid 1 symptomatic case of VTE was much higher, 66, because of the lower rate of symptomatic VTE. Whether extended-duration thromboprophylaxis would offer similar benefits in patients who undergo laparoscopic surgery was addressed in a recent RCT that randomly assigned 225 patients who had undergone laparoscopic resection for colorectal cancer to 7 days or 28 days (extended duration) of heparin therapy. Patients underwent compression ultrasonography following completion of 7 days of heparin therapy and were only randomly assigned to short or extended duration if there was no evidence of a DVT. Venous thromboembolism occurred in 9.7% of the patients randomly assigned to the short therapy and 0.9% in the extended-duration group (relative risk reduction, 91%; 95% CI, 0.3–0.99; p = 0.005). There was no significant difference in bleeding rates between the 2 groups.

Notwithstanding this robust evidence base, compliance with extended-duration thromboprophylaxis remains low. Merkow et al examined national adherence with extended (VTE) chemoprophylaxis guideline recommendations after colorectal cancer surgery in Medicare beneficiaries undergoing open colorectal cancer resections in 2008 to 2009. This study found that a postdischarge prescription for an anticoagulant was filled immediately after discharge by 77 (1.5%) patients and that a prescription for LMWH was filled by only 60 (1.2%) patients. Implementing extended-duration prophylaxis requires institutional support for patient education by providers and nursing, as well as for the financial hurdles that may have to be addressed. Literature regarding oral forms of extended prophylaxis is limited, especially in general and colorectal surgery, and thus no recommendations can be established at this time.

6. Patients with IBD are at high risk for DVT and select patients may benefit from extended prophylaxis. Grade of Recommendation: Weak recommendation based on very low-quality evidence, 2C.

There is increasing recognition that some patients who undergo colectomy for benign disease are also at heightened risk for a postdischarge VTE. Wilson et al examined the risk of VTE in patients undergoing colectomy for benign
conditions by using data from National Surgical Quality Improvement Program. They observed that patients undergoing surgery for ulcerative colitis had the highest 30-day VTE rate (2.74%), followed by patients who underwent surgery for colorectal cancer (1.74%). Forty-one percent of the VTE events in the ulcerative colitis cohort occurred postdischarge. Humes et al examined VTE rates in patients undergoing colectomy in a region of the United Kingdom where primary care and hospital administrative data could be linked. It is notable that, in patients who had undergone emergency colectomy, the crude VTE rates were similar for both benign and malignant disease (114.76 events per 1000 person-years versus 120.98 per 1000 person-years; HR, 1.12; 95% CI, 0.56–2.27). A recent study showed that 44% of surgical in-patients who developed VTE did not receive prophylaxis and these proportions were similar to those in the non-IBD population. In this study, the most common reason cited for not receiving prophylaxis in IBD patients were non-IBD population. In this study, the most common reasons cited for not receiving prophylaxis in IBD patients were GI bleeding (21% of inpatients with prophylaxis held) followed by ambulatory status (7%). Although there is a large amount of evidence demonstrating the high VTE risk in IBD patients, no RCTs have specifically assessed the efficacy of anticoagulation in reducing the rate of VTE in IBD patients or in applying extended-duration prophylaxis after surgery to this population. Nevertheless, in the highest-risk patients, a shared decision-making model is recommended to address this potential complication and its associated morbidity.

REFERENCES

25. Kakkos SK, Caprini JA, Geroulakos G, Nicolaides AN, Stansby GP, Reddy DJ. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of


