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

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The American Society of Colon and Rectal Surgeons (ASCRS) is dedicated to ensuring high-quality patient care by advancing the science and prevention and management of disorders and diseases of the colon, rectum, and anus. The Clinical Practice Guidelines Committee is composed of ASCRS 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 and develop clinical practice guidelines based on the best available evidence. Although not proscriptive, these guidelines provide information on which decisions can be made and do not dictate a specific form of treatment. These guidelines are intended for the use of all practitioners, health care workers, and patients who desire information on the management of the conditions addressed by the topics covered in these guidelines. These 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 considering all the circumstances presented by the individual patient.

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Dis Colon Rectum 2023; 66: 1162–1173
DOI: 10.1097/DCR.0000000000002975

STATEMENT OF THE PROBLEM

In patients undergoing colorectal surgery, the incidence of venous thromboembolism (VTE) may be as high as 13%.[1–5] The true incidence of this condition remains elusive because none of these studies reported the low-end estimate of incidence, and many patients included in these figures may have an asymptomatic deep vein thrombosis (DVT) found on screening. Although clinical efforts focus on VTE prevention in the immediate perioperative period, postdischarge extended prophylaxis is also important, given that many VTEs are diagnosed after hospital discharge.[4]

Several perioperative, intraoperative, and disease-related risk factors contribute to the increased risk of VTE in patients undergoing colorectal surgery.[6–9] Well-described perioperative risk factors include preoperative hospitalization, emergency surgery, BMI >35 kg/m^2, corticosteroid use, comorbidities, anastomotic leak, ileus, and return to the operative room.[10–14] Intraoperative risk factors include more distal resections and prolonged or extensive operations, whereas a minimally invasive surgical approach is protective.[9,10,12,14–19]

Underlying disease diagnoses are another important contributor to VTE risk in patients undergoing colorectal surgery. Patients with colorectal cancer continue to be at increased risk for VTE 1 year postoperatively, especially when receiving chemotherapy.[1] Interestingly, the reported risk of VTE is also high in certain otherwise benign conditions; patients with IBD have a 2- to 3-fold increased risk of DVT and pulmonary embolism (PE) compared with the general population.[20] In hospitalized patients with IBD, the overall risk of VTE has been reported to be 4.3%.[21–24] In a cohort study of 80,445 hospital discharges of patients with IBD, the cumulative rate of VTE at 12 months was 2.1% for patients with Crohn's disease (CD; 1.2% for surgical patients and 2.4% for nonsurgical patients; $p < 0.001$) and 2.0% for patients with ulcerative colitis (UC; 2.2% for surgical patients and 2.0% for nonsurgical patients; $p = 0.32$).[25] Another retrospective, population-based study of those undergoing elective colectomy found a higher rate of 30-day VTE in patients with UC compared to patients with colorectal cancer (OR 2.1; 95% CI, 1.61–2.62; $p < 0.0001$).[26]

These clinical practice guidelines aim to present and grade the evidence for risk stratification and prevention of VTE for those undergoing colorectal surgery. It is important for the reader to distinguish that some of the studies report clinically symptomatic VTE, whereas others report asymptomatic screened VTE, and this distinction needs to be taken into account when interpreting this literature.

METHODOLOGY

These clinical practice guidelines are an update of the guidelines previously published in 2018.[27]

A systematic search was conducted under the guidance of a medical librarian. A search of MEDLINE, PubMed, and the Cochrane Database of Systematic Reviews was initially completed on July 1, 2021, and updated on December 19, 2022 (see Appendix 1 at https://links.lww.com/DCR/C209). This search included search terms and headings from the previously published clinical practice guidelines.[27] Search terms included venous thromboembolism ("venous thromboembolism OR venous thrombosis OR pulmonary embolism OR DVT OR VTE OR PE"); risk assessment ("risk factors OR risk assessment"); Prophylaxis ("prophylaxis OR thromboprophylaxis OR pharmacoprophylaxis OR mechonoprophylaxis OR chemoprophylaxis OR anticoagulants OR early ambulation OR intermittent pneumatic compression devices OR [prevent AND thrombosis OR embolic OR DVT OR VTE OR PE OR thromboembolic]"); surgery ("surgery OR digestive surgical procedures OR colectomy OR proctectomy OR surgeons OR perioperative care OR perioperative period OR preoperative care OR postoperative complications"); colorectal disease ("colorectal surgery OR colectomy OR proctectomy OR rectum OR colon OR rectal OR anal OR anorectal OR inflammatory bowel disease OR Crohn's disease OR ulcerative colitis OR diverticular disease); ambulatory surgery ("ileostomy OR TAMIS OR transanal minimally invasive surgery OR transanal surgery OR ambulatory OR outpatient").

Supplemental searches using related articles and bibliographies were also completed. The search dates were limited from January 1, 2017, to December 19, 2022 (date of most current search). The updated search identified 394 new references. Directed searches of the embedded references from the primary articles were also performed. An additional 22 references were identified through reference review. Thus, a total of 416 unique references were screened. Of the original screened, 98 underwent full-text review by at least 2 coauthors. Fifty-three of these articles were excluded, which left 49 new references in addition to 38 references from the previous clinical practice guidelines (Fig. 1).

CERTAINTY OF EVIDENCE

The final grade of recommendation and level of evidence for each statement were determined using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) system.[28] The certainty of evidence reflects the extent of our confidence in the estimates of effect. Evidence from randomized controlled trials (RCTs) start as high certainty, and evidence from observational studies start as low certainty. The evidence is graded for each outcome as high, moderate, low, or very low (Table 1). Recommendations are influenced by considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty of evidence based on observational studies can be rated up when there is a large magnitude of effect or dose–response relationship. As per GRADE methodology, recommendations are labeled as "strong" or "conditional." Current recommendations are summarized in Table 2. When the 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 entire Clinical Practice Guidelines Committee reviewed recommendations formulated by the subcommittee. The submission was then approved by the ASCRS Executive Council and peer reviewed in

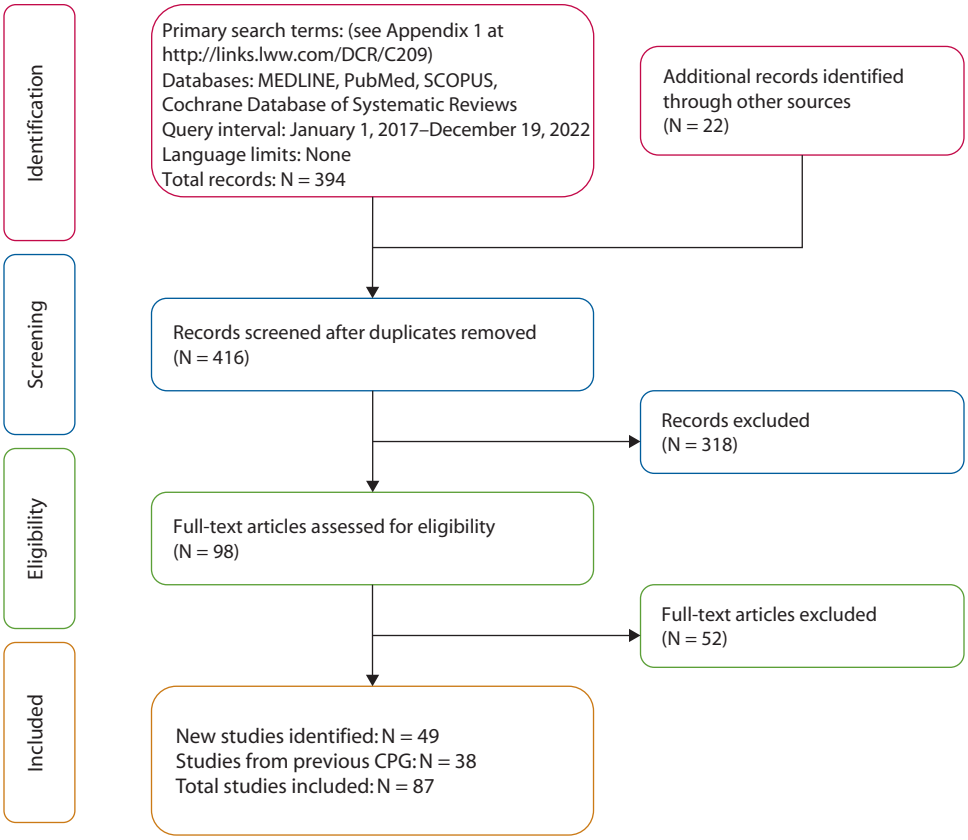

FIGURE 1. PRISMA literature search flowsheet. CPG = clinical practice guidelines; PRISMA = Preferred Reporting Item for Systematic Reviews and Meta-Analysis.

TABLE 1. Interpretation of strong and conditional recommendations using the GRADE approach

Recommendations	*Interpretation*
Strong	Most individuals should receive intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.
Conditional	Different choices will be appropriate for individual patients consistent with their values and preferences. Use shared decision-making. Decision aids may be useful in helping patients make decisions consistent with their indiuals risks, values, and preferences.
GRADE certainty rankings	
High	The authors are confident that the true effect is similar to the estimated effect
Moderate	The authors believe that the true effect is probably close to the estimated effect
Low	The true effect might be markedly different from the estimated effect
Very low	The true effect is probably markedly different from the estimated effect

GRADE = Grading of Recommendations, Assessments, Development, and Evaluation.

Diseases of the Colon and Rectum. Each ASCRS Clinical Practice Guideline is generally updated approximately every 5 years. No funding was received for preparing this guideline, and the authors have declared no competing interests related to this material. This guideline conforms to the Appraisal of Guidelines for Research and Evaluation checklist.

Risk Stratification

1. VTE risk scores may be used when individuals are undergoing colorectal surgery to allow for an informed discussion regarding the risks and benefits of VTE prophylaxis. Strength of recommendation: strong based on low-quality evidence

According to the ninth edition of the American College of Chest Physicians Antithrombotic and Prevention of Thrombosis guidelines, VTE risk levels are classified as very low, low, moderate, and high risk representing an estimated VTE risk of 0.5%, 1.5%, 3.0%, and 6.0%, respectively.[29,30] Risk classification is typically based on either the Rogers or Caprini scores, which are calculated using a variety of risk factors recognizing that up to 40% of hospitalized patients have 3 or more VTE risk factors.[31,32] The original study describing the Rogers score evaluated

TABLE 2. Summary and strength of GRADE recommendations

Summary	*Recommendation strength*	*GRADE quality of evidence*
1 VTE risk scores may be used when individuals are undergoing colorectal surgery to allow for an informed discussion regarding the risks and benefits of VTE prophylaxis	Strong	Low
2 A clinical decision support system embedded into existing electronic health systems may be considered to improve compliance with inpatient VTE prophylaxis recommendations	Strong	Low
3 Mechanical strategies may be used in patients undergoing colorectal surgery, especially in those with a contraindication to chemical prophylaxis	Strong	Moderate
4 Early postoperative mobilization and/or physical therapy may be incorporated into recovery pathways after colorectal resection	Conditional	Very low
5 Inpatient pharmacologic thromboprophylaxis should be given to patients undergoing colorectal surgery who are considered moderate to high risk for VTE and are not at high risk for bleeding complications	Strong	High
6 In patients with an increased risk of VTE and a contraindication to chemoprophylaxis, routine use of inferior vena cava filters is not recommended	Conditional	Very low
7 Routine mechanical or chemical VTE prophylaxis is not recommended in patients undergoing ambulatory colorectal surgery	Conditional	Very low
8 In patients undergoing a colorectal cancer resection deemed to be at high risk of VTE, extended-duration pharmacological thromboprophylaxis may be considered	Conditional	High
9 In patients undergoing colorectal resection for IBD deemed to be at high risk of VTE, extended-duration pharmacological thromboprophylaxis may be considered	Conditional	Very low
10 When extended VTE prophylaxis is recommended, the duration of prophylaxis remains unknown	Conditional	Very low

GRADE = Grading of Recommendations, Assessments, Development, and Evaluation; VTE = venous thromboembolism.

182,783 patients from 128 veteran affairs medical centers and 14 private-sector hospitals who underwent major general or vascular procedures over 2 years (2002–2004).[31] The overall VTE risk was 0.63% (n = 1162). In GI surgery, the risk was 0.93%, accounting for 39% of all VTEs. On multiple logistic regression analysis, 15 risk factors, including GI surgery, were found to be independently associated with VTE and were then used to develop a predictive model for postoperative VTE.[31] Notable limitations of this work include a lack of risk stratification based on colorectal versus small-bowel resection and minimally invasive versus open surgical techniques.

The Caprini score is a well-described risk prediction tool.[32,33] It has been validated by assessing 8216 general, vascular, and urologic surgery inpatients using data from the National Surgical Quality Improvement Program (NSQIP) over 7 years.[30] Several observational studies assessing the ability of the Caprini score to predict VTE among patients undergoing colorectal surgery[34–37] demonstrated an association between Caprini score and VTE with an area under the receiver operating characteristic curve between 0.656 and 0.839. In a prospective study of 148 patients undergoing laparoscopic colorectal cancer surgery, the overall screened VTE risk at postoperative day 6 was 24%; the highest risk was in patients with a Caprini score of 12 or more (40.5%) and between 9 and 12 (20.4%).[34] An additional prospective study of 80 patients with colorectal cancer who received routine postoperative VTE prophylaxis (enoxaparin and compression stockings) found that a cutoff in the Caprini score of 11 resulted in a sensitivity of 76.2% and the specificity of 74.6% in predicting postoperative VTE.[36] A retrospective population-based study of 17,774 surgical patients who received "standard prophylaxis" found a VTE rate of 0.8% and increased Caprini scores were found to be associated with VTE risk (score 0–1: 0.2%; score 2: 0.4%; score 3–4: 0.7%; score 5–6: 1.4%; score 7–8: 2.0%; score 9 or more: 3.3%). The authors concluded that a Caprini score of 5 or more was a reliable criterion for identifying patients with an increased risk for VTE.[37]

2. A clinical decision support system embedded into existing electronic health systems may be considered to improve compliance with inpatient VTE prophylaxis recommendations. Strength of recommendation: strong based on low-quality evidence

Despite well-described risk factors for VTE, clinicians do not uniformly use risk stratification tools or use them incorrectly, potentially underestimating the VTE risk.[38,39] A clinical decision support system (CDSS) embedded into existing electronic health systems has been shown to improve compliance with VTE prophylaxis recommendations. A CDSS was assessed in a meta-analysis of 11 observational studies (9 prospective, 2 retrospective) with 156,366 patients (104,241 in the intervention group and 52,125 in the control group). The use of a CDSS was associated with a significant increase in the rate of ordering appropriate VTE prophylaxis (OR 2.35; 95% CI, 1.78–3.10; $p < 0.001$) and a significant decrease in VTE events (relative risk (RR) 0.78; 95% CI, 0.72–0.85; $p < 0.001$).[40]

Mechanical Prophylaxis and Early Mobilization

3. Mechanical strategies may be used in patients undergoing colorectal surgery, especially in those with a

contraindication to chemical prophylaxis. Strength of recommendation: strong based on moderate-quality evidence

A Cochrane Review of RCTs, including 19 studies assessing surgical patients and 1 study assessing medical patients, demonstrated that graduated compression stockings (GCS) reduced the incidence of VTE. This review found a reduction in any DVT (OR 0.35; 95% CI, 0.28–0.43; $p < 0.001$; 20 studies; n = 2853), proximal DVT (OR 0.26; 95% CI, 0.13–0.53; $p < 0.001$; 8 studies, n = 1035), and PE (OR 0.38; 95% CI, 0.15–0.96; $p = 0.04$; 5 studies; n = 569) compared with the control group.[41]

Although some consensus statements support the use of GCS in addition to chemical prophylaxis, others have not.[42] A recent systematic review assessing the risk of VTE after abdominal or orthopedic surgery found that the risk of VTE was higher in patients who had both extended postoperative prophylaxis (>21 days) and GCS (1.6%; 95% CI, 0.03%–5.4%) compared with those who had extended prophylaxis alone (0.8%; 95% CI, 0.5–1.20). It is important to note that the review used pooled results, and no single study in this analysis compared extended prophylaxis alone with extended prophylaxis plus GCS.[43] However, a recent noninferiority RCT of 1905 patients did compare GCS plus in-hospital low-molecular-weight heparin (LMWH) versus LMWH alone. The trial reported a VTE rate of 1.4% in patients treated with GCS plus LMWH compared with 1.7% in patients treated with LMWH alone (risk difference 0.3%; 95% CI, 0.65%–1.26%). The a priori noninferiority margin was 3.5%, and patients treated with LMWH alone were considered noninferior to patients treated with LMWH plus GCS (test of noninferiority; $p < 0.001$).[44]

Intermittent pneumatic compression (IPC) devices influence the VTE rate by decreasing venous stasis and promoting fibrinolysis. The 2019 Clinical Practice Guidelines from the International Initiative on Thrombosis and Cancer reviewed an RCT (n = 682) of those undergoing gastrectomy for gastric cancer, which found a higher VTE rate when using IPC alone compared to IPC plus LMWH (3.6% vs 0.6%; $p = 0.008$). However, 2 small RCTs (n = 30 with gynecologic malignancy and n = 90 with thoracic malignancies) showed no change in VTE rates when adding chemoprophylaxis to IPC.[45] A meta-analysis of 5 RCTs with 3133 patients showed a reduced VTE incidence when comparing IPC alone versus no treatment (OR 0.36; 95% CI, 0.18–0.71) but did not demonstrate a difference when comparing chemoprophylaxis versus IPC (OR 0.82; 95% CI, 0.48–1.37), chemoprophylaxis versus chemoprophylaxis plus IPC (OR 0.87; 95% CI, 0.49–1.53), or IPC versus chemoprophylaxis plus IPC (OR 0.95; 95% CI, 0.52–1.69).[46] A more recent RCT, which was not included in the meta-analysis, accrued patients at high risk of VTE (Caprini score more than 11) who underwent major surgery.[47] This study included 278 patients who were randomly assigned to either IPC plus standard prophylaxis with GCS versus standard prophylaxis alone. IPC with chemoprophylaxis reduced the incidence of DVT compared to standard prophylaxis (LMWH) with GCS alone (0.5% vs 16.7%; $p < 0.001$).[47]

4. Early postoperative mobilization and/or physical therapy may be incorporated into recovery pathways after colorectal resection. Strength of recommendation: conditional based on very low-quality evidence

Given the association between immobilization and VTE risk, strategies for early postoperative mobilization have been investigated.[48,49] However, there is a lack of high-quality evidence to support early ambulation for VTE prevention. One study implemented a standardized mobilization order for patients to be "out of bed" at least 3× daily beginning the day of surgery. This study included 1569 patients before implementation and 1323 patients after implementation. Postimplementation, the risk of DVT decreased from 1.9% to 0.3% ($p < 0.01$) and that of PE decreased from 1.1% to 0.5% ($p < 0.01$). The risk-adjusted VTE rate declined from a preimplementation OR of 3.41 to a postimplementation OR of 0.94 ($p < 0.05$).[50]

There are no trials that directly compare early mobilization and/or physical therapy with alternative VTE risk modification strategies. A randomized study[51] compared LMWH plus physical therapy (n = 199) to physical therapy alone (n = 201) in patients undergoing laparoscopic gastric, colon, or rectal resections and demonstrated VTE in 1.2% of patients who received LMWH plus physical therapy versus 4.0% with physical therapy alone, but the difference was not statistically significant.[51]

Inpatient and Early Postoperative Thromboprophylaxis

5. Inpatient pharmacologic thromboprophylaxis should be given to patients undergoing colorectal surgery who are considered moderate to high risk for VTE and are not at high risk for bleeding complications. Strength of recommendation: strong based on high-quality evidence

Benefits of Pharmacologic Prophylaxis

The benefits of pharmacologic prophylaxis with LMWH or low-dose unfractionated heparin (LDUH) in patients undergoing colorectal surgery were assessed in a 2003 Cochrane Review and another meta-analysis several years later.[52,53] The more recent meta-analysis of 11 RCTs included 306 patients in the LMWH/LDUH group and 335 patients in the placebo/no treatment group.[53] After pooling the data, LMWH/LDUH therapy effectively reduced the risk of VTE (OR 0.32; CI, 0.20–0.53). A seminal meta-analysis of more than 70 RCTs comparing LDUH with placebo (>16,000 patients) across several surgical subspecialties demonstrated that LDUH therapy was associated with a significantly reduced incidence of screened DVT

(22% vs 9%; $p < 0.001$), and a reduction in the incidence of PE (1.6% vs 0.90%; $p < 0.02$).[54] Within the subset of patients in this study who underwent general surgery, LDUH was typically 5 to 7 days. An additional meta-analysis comparing LMWH with no prophylaxis after patients undergoing general surgery found that LMWH reduced the risk of both clinical VTE (RR 0.29; 95% CI, 0.11–0.73) and asymptomatic DVT (RR 0.28; 95% CI, 0.14–0.54).[55] In patients undergoing major general surgery procedures, the American Society of Hematology (ASH) performed a meta-analysis and found a reduced risk of symptomatic PE (RR 0.45; 95% CI, 0.23–0.88; 11 studies; moderate certainty of evidence) and proximal DVT (RR 0.38; 95% CI, 0.14–1.00; 6 studies; very low certainty of evidence) with pharmacologic prophylaxis.[56]

Results from recently published randomized trials from Japan have questioned the benefits of routine chemoprophylaxis after laparoscopic surgery. An RCT of inpatients who underwent laparoscopic resection for gastric cancer (n = 174), colon cancer (n = 162), or rectal cancer (n = 112) compared IPC with enoxaparin to IPC alone. There was no difference in the overall screened VTE risk between patients treated with or without enoxaparin (3.3% vs 4.8%; $p = 0.45$). Outcomes for patients with colon and rectal cancer were not reported separately, and VTE was only assessed on postoperative day 7 by multidetector CT.[57] A similar trial enrolled 121 patients undergoing laparoscopic colorectal resections and found no difference in the VTE incidence at 28 days (12.3% in the enoxaparin + IPC group vs 11.9% in the IPC alone group; $p = 1.0$).[58] Another RCT from Japan compared enoxaparin plus physiotherapy to physiotherapy alone in 400 patients undergoing laparoscopic resection for gastric, colon, or rectal cancer.[51] In this study, there was no difference in screened VTE (by CT or ultrasonography) at 7 days between the 2 groups (1.2% vs 4.0%; OR 0.3; 95% CI, 0.03–1.53). Other retrospective studies such as a retrospective review of patients from the Michigan Surgical Quality Collaborative examining 32,856 patients having non–orthopedic surgery (6067 patients undergoing colectomy) did not show a decrease in postoperative VTE in patients treated with pharmacologic VTE prophylaxis.[59] Ultimately, these results need to be interpreted in the context of the RCTs and Cochrane analysis to determine whether to use pharmacologic VTE prophylaxis in a given patient.

Risks of Pharmacologic Prophylaxis

Evidence suggest that there is an increased risk of bleeding in the setting of pharmacologic prophylaxis. A meta-analysis of more than 12,000 general surgery, urology, and orthopedic postoperative patients found that LDUH was associated with increased excessive bleeding or need for transfusion compared with no pharmacologic prophylaxis (5.9% vs 3.8%).[54] The 2019 ASH guideline and meta-analysis for preventing VTE supported this finding and found an increased bleeding risk in surgical patients receiving pharmacologic prophylaxis compared with those who did not (RR 1.37; 95% CI, 0.89–2.13; 12 studies, moderate certainty of evidence).[56] An additional meta-analysis including 8 RCTs and 5520 patients found an increased risk of wound hematoma (RR 1.88; 95% CI, 1.54–2.28) in patients who received LMWH versus placebo or nothing.[55] Finally, in an RCT of 448 patients undergoing laparoscopic resection for gastric, colon, or rectal cancer, there was an increased risk of bleeding in patients treated with enoxaparin and IPC versus IPC alone (5.4% vs 0%). However, in this trial, only 1 bleeding event required intervention with a transfusion.[57]

LMWH Versus LDUH

The ASH review and meta-analysis[56] identified several clinical trials comparing LMWH to LDUH in major general surgery. Although the quality of evidence was low, there was no significant difference in symptomatic PE (RR 0.83; 95% CI, 0.58–1.19; 31 studies) or proximal DVT (RR 1.01; 95% CI, 0.20–5.00; 6 studies) between patients treated with LMWH or LDUH. There was also no difference in major bleeding (RR 0.97; 95% CI, 0.78–1.20; 34 studies). The Canadian Colorectal DVT Prophylaxis Trial included 936 patients, and it confirmed that LMWH (enoxaparin 40 mg/day) was as effective and safe as LDUH (5000 units every 8 hours) in VTE prevention after colorectal surgery. In this RCT, the incidence of screened VTE on bilateral venography was 9.4% in both groups, and the rate of proximal DVT was 2.6% in the LDUH group and 2.8% in the LMWH group.[3] However, this study also reported more overall bleeding events in patients who received LMWH versus LDUH (10.4% vs 6.5%; $p = 0.02$), but there was no significant difference in major bleeding events.

A Cochrane Review of 4 RCTs (n = 1183 patients) compared LDUH (5000 Units) and LMWH (2500–3000 Units of anti-Xa or 40 mg of enoxaparin) and found that the 2 treatments were equally effective in preventing VTE (OR 1.01; 95% CI, 0.69–1.52).[52] All 4 trials used 1 preoperatively dose, with prophylaxis continued up to 10 days postoperatively.

Although not specific to colorectal or abdominopelvic surgery, a meta-analysis of 12 RCTs and 3 prospective observational studies compared the risk of heparin-induced thrombocytopenia, in those receiving either LDUH or LMWH. These articles were published between 1986 and 2002 and included between 52 and 1427 patients. This meta-analysis found lower odds of heparin-induced thrombocytopenia in those receiving LMWH (OR 0.10; 95% CI, 0.03–0.33; $p < 0.001$; I^2 0%).[60]

Furthermore, the ASH recommends LMWH or fondaparinux over unfractionated heparin in those undergoing cancer surgery for inpatient prophylaxis as a conditional recommendation based on low certainty of the evidence.[61]

Pharmacologic Prophylaxis Alternatives to LDUH or LMWH

The American College of Chest Physicians Guidelines reviewed alternatives to LMWH and LDUH in patients undergoing non–orthopedic surgery, including fondaparinux and high-dose aspirin.[29] In an RCT of over 2800 patients undergoing major abdominal surgery (including more than 1600 patients undergoing colorectal surgery), fondaparinux was found to have similar efficacy in reducing the risk of VTE compared with LMWH (RR 0.75; 95% CI, 0.52–1.09) and risk of nonfatal major bleeding (RR 1.12; 95% CI, 0.94–1.34).[62] There was no difference in overall VTE risk (4.6% vs 6.1%; $p = 0.14$) or major bleeding (3.4% vs 2.4%; $p = 0.12$).[62] In a meta-analysis of more than 2800 patients undergoing general surgery, high-dose aspirin was similarly found to reduce the risk of VTE compared with no prophylaxis (RR 0.63; 95% CI, 0.47–0.79), and also resulted in a higher risk of major bleeding (RR 1.39; 95% CI, 1.12–1.74).[63]

6. In patients with an increased risk of VTE and a contraindication to chemoprophylaxis, the routine use of inferior vena cava filters is not recommended. Strength of recommendation: conditional based on very low-quality of evidence

There is a paucity of data examining the use of inferior vena cava (IVC) filters in elective colorectal surgery. In fact, an updated Cochrane Review from 2020 about filters preventing PE included no new studies related to IVC filters in colorectal surgery, and the one study on patients with cancer that was incorporated into this review included nonsurgical patients with an established diagnosis of DVT/PE.[64]

In the trauma literature, a meta-analysis reported a significantly lower pooled OR of having a PE (OR 0.21; 95% CI, 0.09–0.49) in patients with an IVC filter placed compared with matched historical controls.[65] However, the analysis concluded that no strong conclusions could be made, given the lack of contemporary use of chemoprophylaxis across the studies. Another large trauma study of 35,658 patients in which 847 (2%) received a prophylactic IVC filter found no difference in PE rate with or without an IVC filter (0.4% in both groups) but noted an increased risk of DVT in the IVC filter group (3.9% vs 0.6% without a filter; $p < 0.0001$).[66] The PREPIC trial was an RCT of 400 patients at high risk for PE with a documented proximal DVT with or without PE who received standard anticoagulation with or without an IVC filter.[67] At 8 years, IVC filters significantly reduced the risk of PE, increased the risk of DVT (35.7% vs 27.5%; $p = 0.042$), and had no impact on mortality at 8 years (48.1% vs 51.0%; $p = 0.83$).

Consistent with the previously mentioned findings, the consensus guidelines from the ASH in 2019 recommended against the use of prophylactic IVC filters in patients undergoing surgery who have a contraindication to anticoagulation based on their meta-analysis. In this setting, there is an increased risk of mortality (RR of 1.38; 95% CI, 0.81–2.37) and increased risk of proximal DVT (RR 2.19; 95% CI, 1.07–4.50) without a decrease in symptomatic PE with IVC placement.[56] Also, studies have underscored the importance of an IVC filter retrieval plan to avoid complications from a long-dwelling IVC filter.[68] It is important to note that the previously quoted studies may have limited applicability to the colorectal surgery population, given that the analyzed data included only trauma and bariatric patients.

7. Routine mechanical or chemical VTE prophylaxis is not recommended in patients undergoing ambulatory colorectal surgery. Strength of recommendation: conditional based on very low-quality evidence

Patients undergoing ambulatory colorectal surgery are typically considered low risk for VTE. This assessment is based on the usually short duration and elective nature of this surgery and the minimal use of general anesthesia and patient positioning involved in these cases.[27] Notably, no studies have assessed the use of mechanical or pharmacologic prophylaxis in this population of patients. The risk of VTE in ambulatory surgery was investigated in a large NSQIP study of nearly 2 million patients who underwent outpatient procedures.[69] The overall rate of VTE was 0.19%, and the rate of VTE increased with a longer surgical duration.

Extended VTE Prophylaxis

8. In patients undergoing a colorectal cancer resection, extended-duration pharmacologic thromboprophylaxis may be considered. Strength of recommendation: conditional based on high-quality evidence

Abdominal or Pelvic Surgery and Extended Prophylaxis

A 2019 Cochrane Review included the results of 7 RCTs with 1728 patients, including 1257 patients with cancer. This review compared extended thromboprophylaxis of at least 14 days postoperatively to shorter inpatient-only–based protocols in patients undergoing GI, gynecology, or urologic surgery. The incidence of screened VTE was 13.2% in the control group compared with 5.3% in the extended thromboprophylaxis group (OR 0.38; 95% CI, 0.26–0.54; $p < 0.0001$; moderate-quality evidence). The risk of symptomatic VTE was low in each group (0.1% vs 1.0%) and was not statistically different between groups (OR 0.30; 95% CI, 0.08–1.11; $p = 0.07$; moderate-quality evidence). Notably, there was no difference in mortality (OR 1.15; 95% CI, 0.72–1.84; moderate-quality evidence).[70] A large systematic review assessing patients with cancer undergoing abdominopelvic surgery has also been published.[71] This review identified 6 RCTs, 7 meta-analyses, and 5 nonrandomized cohort studies assessing the risks and benefits

of extended prophylaxis versus standard prophylaxis after surgery. The authors found significantly reduced rates of any VTE (both asymptomatic and symptomatic) in the extended prophylaxis group. It should be noted that the study authors did not attempt to perform a quantitative analysis and instead provided a narrative analysis of the included studies. An additional systematic review of 1 RCT[72] and 3 nonrandomized studies[73–75] of 3198 patients undergoing open pelvic surgery for malignancy compared inpatient only versus extended thromboprophylaxis and found no difference in VTE risk (RR 1.55; 95% CI, 0.81–2.95; $p = 0.18$; based on low-quality evidence).[76]

The ASH 2019 guidelines also presented a meta-analysis comparing patients undergoing major abdominal surgery with chemoprophylaxis continuing for a short course (4–14 days) versus extended prophylaxis (19–42 days). This meta-analysis included 20 studies assessing at least 1 VTE-related end point in patients undergoing any major surgery. They found a likely reduction in symptomatic PE (RR 0.44; 95% CI, 0.22–0.85; moderate certainty in the evidence), a reduction in symptomatic DVT (RR 0.30; 95% CI, 0.21–0.42, moderate certainty of evidence), and no difference in rates of major bleeding (RR 1.00; 95% CI, 0.59–1.70; low certainty of evidence).[56]

An important limitation of the previously mentioned guidelines is that most recommendations were based on at least 7 days of inpatient postoperative thromboprophylaxis.[54,55] With the increasing utilization of minimally invasive surgery and enhanced recovery programs, many patients undergoing colorectal surgery are discharged before postoperative day 7; it may be difficult to extrapolate these results when managing patients undergoing contemporary surgery.

Colorectal Cancer Surgery and Extended Prophylaxis

A trial of 225 patients undergoing laparoscopic colorectal cancer surgery randomly assigned patients to either 7 days (short duration) or 28 days (extended duration) of LDUH. All patients underwent compression ultrasonography after the first 7 days of heparin therapy and were eligible for inclusion in the study if there was no DVT. VTE at 3 months occurred in 9.7% of the patients (n = 11/113) in the short-duration group and in 0.9% of the patients (n = 1/112) 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. This study was terminated early because of the significant VTE reduction in the extended treatment arm.[77] In contrast, the PERIOP-01 trial did not find a benefit of extended VTE prophylaxis.[78] This larger study randomly assigned 614 patients to either 8 weeks of tinzaparin (an LMWH) or a placebo at the time of hospital discharge. Approximately 70% of patients underwent laparoscopic surgery, and an equal number of patients with colon cancer and rectal cancer were included. This study found that the risk of VTE at 3 months was 1.7% (n = 5/299) in the tinzaparin group compared to 1.3% (4/303) in the control group ($p = 0.7$).[79] It should be noted that the outcome was symptomatic or incidentally found VTE and not screened VTE.

Finally, the PRO-LAPS study randomly assigned 582 patients undergoing laparoscopic colorectal cancer surgery. In this study, all patients were initially assigned to receive 7 days of LMWH and were then randomly assigned to 21 days of either rivaroxaban (a direct oral anticoagulant) or placebo.[80] At 28 days postoperatively, the screened VTE risk was 1.0% (n = 3/287) in the rivaroxaban group compared with 3.9% (n = 11/282) in the control group ($p = 0.03$).

The previously discussed trials are most pertinent to the modern management of colorectal cancer surgical patients and were the basis of the recommendation. This literature needs to be interpreted cautiously because many of these studies cited screened but not symptomatic VTE, and the optimal duration of prophylaxis is unclear. The cost-benefit of extended prophylaxis for those undergoing colorectal surgery has been assessed in several studies.[81–83] Ianuzzi et al modeled the cost-benefit of those undergoing major oncologic abdominal surgery. This work demonstrated a cost-benefit of extended prophylaxis (21 days) if the VTE risk was more than 2.39%, based on a $50,000/QALY threshold.[81] Additional studies assessed patients undergoing surgery for IBD.[82,83] Each of these studies did not demonstrate cost-benefit based on findings of $257,280/QALY to $1.9 million/QALY.

9. In patients undergoing colorectal resection for IBD deemed to be at high risk of VTE, extended-duration pharmacologic thromboprophylaxis may be considered. Strength of recommendation: conditional based on very low-quality evidence

IBD or Other Benign Conditions and Extended Prophylaxis

The reported risk of VTE can be as high in some otherwise benign conditions as in colorectal cancer. A population-based retrospective cohort study from the United Kingdom found similar VTE rates in patients undergoing emergency colectomy for benign and malignant disease (114.76 events per 1000 person-years vs 120.98 per 1000 person-years, respectively; HR, 1.12; 95% CI, 0.56–2.27).[84] In addition, it has been well described that patients with IBD have a 2- to 3-fold increased risk of DVT and PE compared with the general population.[20] In hospitalized patients with IBD, the overall risk of VTE has been reported to be 4.3%.[21–24] A systematic review of 11 observational studies, which included mostly population-based studies, found an overall risk ratio of 2.03 (95% CI, 1.72–2.39) for VTE in patients with IBD versus those without IBD.[85] A population-based cohort study from Ontario,

Canada, included 80,445 hospital discharges of patients with IBD and found that the cumulative rate of VTE at 12 months was 2.1% for patients with CD (1.2% for surgical patients and 2.4% for nonsurgical patients; $p < 0.001$) and 2.0% for patients with UC (2.2% for surgical patients and 2.0% for nonsurgical patients; $p = 0.323$).[25] A NSQIP study of patients undergoing colectomy for the benign disease found that patients with UC had an increased 30-day VTE rate (2.74%) compared to patients with colorectal cancer (1.74%). After adjusting for confounders on multivariable analysis, patients with UC had increased odds of VTE in comparison with patients with cancer (OR 2.1; 95% CI, 1.61–2.62; $p < 0.001$). Notably, 41% of the VTE events in the UC cohort occurred after discharge from the hospital.[26]

No RCTs or high-quality observational studies have assessed extended VTE prophylaxis exclusively in patients undergoing colorectal surgery for otherwise benign pathology. In the Cochrane Review described previously,[70] 2 RCTs included both benign and malignant indications but did not perform a subgroup analysis of those with benign pathology only.[86,87]

10. When extended VTE prophylaxis is recommended, the duration of prophylaxis remains unknown. Strength of recommendation: conditional based on very low-quality evidence

The postoperative extended thromboprophylaxis assessed in the aforementioned clinical trials ranged between 14 and 56 days. There are no studies directly comparing the duration of extended prophylaxis. Thus, optimal duration has not yet been determined.

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