Eline Naert / Department of Medical Oncology

Prophylaxis and treatment of venous thrombo-embolic events in patients with solid tumors

Post-MASCC
27/11/2020

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METHODOLOGY

Pubmed
Last 5 years
Guidelines and/or systematic reviews

Some restrictions….

Only valid for solid tumors
Only valid for adult cancer patients
Guidelines are the summit of ready-to use material but lack nuances

NCCN

ASCO

ITAC

ASH

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	NCCN	ASCO	ITAC	ASH
Year of Publication	2020	2019	2019	2018/2019
Published in	NCCN website	Journal of Clinical Oncology (IF = 32)	Lancet Oncology (IF = 33)	Blood advances (IF = NA)
Methodology	Panel meeting & voting	Systematic review In Pubmed & Cochrane Library – Expert Panel	GRADE In several databases Working group	GRADE
Search interval	Continuous	August 1, 2014, and December 4, 2018	January 1, 2015, and December 31, 2018	Until February/March 2017
Levels of evidence	Categories of evidence and consensus Category 1 / 2A / 2B / 3	Type: EB = evidence based Inf = informal consensus Evidence quality: Int = intermediate Ins = insufficient Strength of recommendation: Mod = moderate Strong	Levels of evidence: High = A Moderate = B Low = C Very low = D Levels of recommendation: Strong = grade 1 Weak = grade 2 Best clinical practice = guidance	Strong recommendation interpretation for clinicians Conditional recommendation interpretation for clinicians

Agreement between guidelines

No clear agreement between guidelines

Clear disagreement between guidelines

PROPHYLAXIS

1/ Should hospitalized patients with cancer receive anticoagulation for VTE prophylaxis?

2/ Should ambulatory patients with cancer receive anticoagulation for VTE prophylaxis during systemic chemotherapy?

3/ Should patients with cancer undergoing surgery receive perioperative VTE prophylaxis?

4/ What is known about risk prediction and awareness of VTE among patients with cancer?

5/ Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival? Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival?

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PROPHYLAXIS

1/ Should hospitalized patients with cancer receive anticoagulation for VTE prophylaxis?

Trend to ‘yes’!

Additional comments:

- After consideration of possible CI’s (bleeding risk?)
- Pharmacologic (LMWH or fondaparinux or UFH) versus mechanic
- Routine pharmacologic thromboprophylaxis should not be offered to patients admitted for minor procedures or chemotherapy infusion

PROPHYLAXIS

2/ Should ambulatory patients with cancer receive anticoagulation for VTE prophylaxis during systemic chemotherapy? *not valid for multiple myeloma patients*

1/ No routine use (ASCO & ITAC)
2/ Use Khorana risk score prior to starting a new chemotherapy (NCCN, ASCO & ITAC)
< 2 = low risk for VTE = no prophylaxis
≥ 2 = intermediate/high risk for VTE = consider prophylaxis by apixaban/rivaroxaban/LMWH up to 6 months
3/ Indicated in locally advanced or metastatic pancreatic cancer treated with systemic therapy (ITAC)
4/ Only in clinical trial for locally advanced or metastatic lung cancer treated with systemic therapy (ITAC)

PROPHYLAXIS

3/ Should patients with cancer undergoing surgery receive perioperative VTE prophylaxis?

In case of ‘high risk’ surgery (ie abdominal/pelvic):

1/ UFH or LMWH with/without intermittent pneumatic compression
2/ Start 2-12h preoperatively
3/ Extended prophylaxis (up to 4 weeks post operatively) (NCCN & ITAC)
For high-risk feature patients (ASCO)

In case of ‘non high risk’ surgery

Case by case decision

* ONLY IN ITAC

PROPHYLAXIS

4/ What is known about risk prediction and awareness of VTE among patients with cancer?

Topics to remember:

- Need of periodical VTE risk assessment
- Individual risk factors, including biomarkers or cancer site, do not reliably identify patients with cancer at high risk for VTE
- Ambulatory setting and treatment with systemic therapy: Risk assessment can be conducted based on a validated risk assessment tool (Khorana score)

 NO INFORMATION ABOUT THIS SUBJECT AVAILABLE AT NCCN WEBSITE

PROPHYLAXIS

5/ Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival? Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival?

No

TREATMENT

1/ What is the best method for treatment of patients with cancer with established VTE to prevent recurrence?

2/ What is the optimal duration for treatment?

3/ What is the place of a V. Cava filter?

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TREATMENT

1/ What is the best method for treatment of patient recurrence?

LMWH:

preferred for patients with gastric or gastroesophageal lesions

VKA's

UFH

DOACs:

preferred for patients without gastroesophageal lesions or genitorurinary bleeding risk

Consider only:
1/ Edoxaban 60 MG PO daily after initial therapy with LMWH or UFH for at least 5 days
2/ Rivaroxaban 15 mg PO BID for the first 21 days followed by 20 MG daily
3/ Apixaban 10 MG PO BID for 7 days followed by 5 mg PO BID

Drug interactions!!!

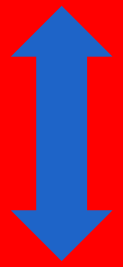
Fondaparinux

TREATMENT

2/ What is the optimal duration for treatment?

NCCN:

At least 3 months or as long as active cancer or cancer therapy



ASCO & ITAC:

At least 6 months

TREATMENT

3/ What is the place of a V. Cava filter?

1/ Lack of evidence
2/ Patients with absolute contraindications to anticoagulant therapy in the acute treatment setting (VTE diagnosis within the past 4 weeks) if the thrombus burden was considered life-threatening.
3/ Patients with progression of thrombosis (recurrent VTE or extension of existing thrombus) despite optimal anticoagulant therapy

SPECIAL SITUATIONS…

1/ What do you do if your patient has a creatinine clearance < 30 mL/min?
2/ What do you do if your patient has liver disease?
3/ What do you do if your patient has thrombocytopenia?
4/ What do you do if your patient is pregnant?
5/ What do you do if there is a recurrence under anticoagulation?
6/ What do you do if there is a catheter related thrombosis?
7/ What do you do if there are CNS metastases?

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SPECIAL SITUATIONS

1/ What do you do if your patient has a creatinine clearance < 30 mL/min?

What not to do?
LMWH: use with caution – consider dose adjustments
Fondaparinux is contraindicated
DOACs are contraindicated

What to do?
Lack of evidence!
Tinzaparin only LMWH without dose reduction requirement
UFH followed by early VKA (possible from day 1)
Anti Xa monitoring LMWH adjusted to anti-Xa level

SPECIAL SITUATIONS

2/ What do you do if your patient has liver disease?

What not to do?

Apixaban/edoxaban are contraindicated when AST/ALT > 2x ULN or total bilirubin > 1,5x ULN.

Dabigatran/rivaroxaban are contraindicated when AST/ALT > 3x ULN

SPECIAL SITUATIONS

3/ What do you do if your patient has thrombocytopenia?

In case you need prophylactic anticoagulation
Platelets < 30.000 - 50.000/mcL is a contraindiciation
Platelets < 20.000/mcL is a contraindication to mechanical prophylaxis
DOACs: when using apixaban, edoxaban or rivaroxaban hold until platelet count recovers to > 50.000/mcL
For patients at high risk for recurrent VTE and anticipated prolonged thrombocytopenia, transfusion of platelets to maintain platelet count of > 25.000/mcL to allow for continuation of enoxaparin may be appropriate

In case you need therapeutic anticoagulation
Platelets < 30.000 - 50.000/mcL is a relative contraindiciation
DOACs: when using apixaban, edoxaban or rivaroxaban hold until platelet count recovers to > 50.000/mcL
For patients at high risk for recurrent VTE and anticipated prolonged thrombocytopenia, transfusion of platelets to maintain platelet count of > 25.000/mcL to allow for continuation of enoxaparin may be appropriate

SPECIAL SITUATIONS

4/ What do you do if your patient is pregnant?

- LMWH for treatment of established venous thromboembolism and for venous thromboembolism prophylaxis
- Avoidance of VKA and DOACs

 NO INFORMATION ABOUT THIS SUBJECT AVAILABLE AT NCCN OR ASCO

SPECIAL SITUATIONS

5/ What do you do if there is a recurrence under anticoagulation?

Lack of evidence
Consider HIT when occurring under UFH, LMWH or fondaparinux

<u>Options to be considered:</u>
1/ for LMWH: Increase LMWH dose by 20-25% or switch to 12-hour schedule or switch to DOACs or switch to fondaparinux
2/ for DOACs: switch to LMWH
3/ for VKAs: switch to LMWH or DOACs
4/ for fondaparinux: switch to UFH, LMWH or DOACs
5/ for UFH: increase UFH dose or switch to LMWH or DOACs

SPECIAL SITUATIONS

6/ What do you do if there is a catheter related thrombosis?

1. Routine prophylaxis is not recommended
2. Anticoagulation with LMWH for at least 3 months or as long as central venous access device is in place.
   Consider longer duration anticoagulation in patients with poor flow, persistent symptoms or unresolved thrombus.
   Consider shorter duration of anticoagulation if clot or symptoms resolve in response to anticoagulation and/or catheter removal

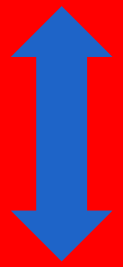
3. Consider catheter removal if symptoms persist or if the catheter is infected or dysfunctional or no longer necessary
4. Consider catheter-directed pharmacomechanical thrombolysis in appropriate candidates
5. In case of contraindication to anticoagulation, the catheter should be removed. In case the contraindication is resolved anticoagulation should be initiated for at least 3 months

SPECIAL SITUATIONS

7/ What do you do if there are CNS metastases?

NCCN:

CNS metastases is a relative contraindication for therapeutic anticoagulation



ASCO:

Anticoagulation as described for other patients with cancer should be offered, although uncertainties remain about choice of agents and selection of patients most likely to benefit

ELINE NAERT
Eline.naert@uzgent.be
Department of Medical Oncology

Universitair Ziekenhuis Gent
C. Heymanslaan 10 | B 9000 Gent
T +32 (0)9 332 21 11
E info@uzgent.be

www.uzgent.be
Volg ons op

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