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Review article

Guidelines for the prevention of venous thromboembolism in hospitalized patients with pelvi-acetabular trauma



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ABSTRACT

Background: Venous thromboembolism is a dreaded complication leading to increased morbidity and mortality in patients having pelvi-acetabular fractures.

Objectives: These evidence based guidelines aim to provide the decision making ability in the prevention of venous thromboembolism in patients with pelvi-acetabular trauma planned for operative or non operative treatment.

Methods: The patients were subclassified into 5 categories. The PICO framework was used to devise research questions in each category. The systematic reviews were performed for each research question. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess outcomes of critical interest. The guideline panel consisting of expert members of different subspecialties, analyzed the evidence and made recommendations.

Results: The guideline panel proposed 21 recommendations. There are five recommendations in category 1 to 3, two recommendations in category 4 and four recommendations in category 5.

Conclusion: In pelvi-acetabular fractures there is strong evidence to suggest that thromboprophylaxis should be given. It should be initiated as early as possible after control of hemorrhage. The chemical prophylaxis is the preferred mode and LMWH is the preferred agent of choice. The mechanical methods can be used as an adjunct. The routine prophylactic use of IVC filters is not recommended. However, the use of retrievable IVC filters in high risk patients with established VTE in preoperative period can be considered. The use of newer directly acting oral anticoagulants is gaining importance.

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Introduction

Aims and objectives

The aim of these guidelines is to provide evidence based recommendations for the prevention of venous thromboembolism

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(VTE) in patients sustaining pelvi-acetabular fractures. The target audience includes patients, Orthopaedic surgeons, general surgeons, anesthetists, pulmonologists, hematologists, pharmacists, nursing staff, and health policy makers (regional, national or international level).

Description of health problem

VTE is a dreaded complication that can lead to fatal outcome in trauma patients. It leads to high morbidity and mortality in patients with pelvi-acetabular trauma. The prevalence of deep vein thrombosis (DVT) varies and is estimated around 60% in patients without any prophylaxis. The risk of pulmonary embolism ranges

between 2 and 10%.² The pulmonary embolism (PE) is third most common cause of death in trauma patients in postoperative period beyond 24 h of admission.³ The incidence of DVT in Indian population has been considered low previously based upon the studies conducted in arthroplasty patients.⁴ However, the studies conducted on the pelvi-acetabular or lower limb fractures were fewer in number but the incidence reported was significantly higher (up to 60%).^{5–8} The prevalence of VTE is more in pelvi-acetabular trauma in comparison to hip arthroplasty. This is attributed to multiple factors including high velocity injury, disruption of pelvic vessels, immobilization for long duration and manipulation during surgical procedure.⁵All the three components of classical triad of Virchow namely circulatory stasis, endothelial damage and hypercoagulability are involved following pelvi-acetabular trauma.

Target population

These guidelines laid focus on adult patients having pelviacetabular trauma who are having potential risk for preoperative as well as postoperative VTE.

Risk assessment for VTE in Pelvic fractures

The Greenfield risk assessment profile (GRAP) is the most widely practiced validated scoring system used in trauma patients. Pelvic fracture is a major risk factor and given 4 points on the GRAP. The scores > 10 on GRAP represent high risk of VTE. A recent study evaluated individual risk factors mentioned in GRAP scoring and proposed a modified score with predictive power similar to the original score. The five variables easily available at bedside (four or more transfusions in the first 24 h, operation > 24 h, Glasgow coma scale, pelvic fracture, and age 40–59 years) can easily assess the risk for VTE in trauma patients. Other Scoring systems like Caprini risk assessment model (CRAM), the Trauma embolic scoring system (TESS) also place Pelvic fractures as a risk factor for VTE and hence it becomes necessary to provide thromboprophylaxis to this high risk group. 11,12

The guideline panel have devised a stepwise approach for decision making in assessment of VTE prophylaxis in Pelvi-acetabular fracture patients.

The patients having Pelvi-acetabular fractures are subclassified into one of these 5 categories defined below.

Category1: Pelvis and acetabular fractures planned to be managed conservatively; Patient Haemodynamicaly stable, no contraindications to chemical prophylaxis and no medical comorbidities.

Category2: Pelvis and acetabular fractures planned for operative management; Patient Haemodynamicaly stable, no contraindications to chemical prophylaxis and no medical co-morbidities. Category3Critically ill patient presenting to emergency department (Ongoing bleeding and high risk of Bleeding).

Category4Patient with established DVT and planned for surgery (Pre-Operative developed DVT).

Category 5: Patient with medical co-morbidities.

The common modalities of VTE prophylaxis in pelvi-acetabular patients have been shown in Table 1.

Methodology

Guidelines panel

The members of guidelines panel include Orthopaedic surgeons practicing pelvi-acetabular subspeciality, anaesthetists with major

trauma as subspeciality, general surgeons involved in trauma and critical care, pulmonologist and Interventional Radiologist.

Formulation of clinical questions and outcome of interest

The authors used PICO framework (Table 2) for the formulation of research questions in each category of patients with pelviacetabular trauma. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was used to select outcomes of interest. ^{13,14} The outcomes were rated as critical or non critical. The outcome of interests include non fatal PE, DVT, mortality and major bleeding. Three databases of PubMed, EMBASE and SCOPUS were searched on July 21, 2020 using Medical subject headings (MeSH) terms. A systematic review was performed and all the studies addressing these important outcomes were included. The summary of finding tables were prepared and the quality of evidence for each outcome was calculated according to the factors outlined in GRADE approach (supplementary materials).

Details of search methodology

Three databases of PubMed, EMBASE and SCOPUS were searched on July 21, 2020 using MeSH terms (Table 3). A total number of 1164 hits were obtained. We also performed a secondary search from the references from all the articles selected as per the predefined criteria.

Studies assessing venous thromboembolism in patients with pelviacetabular trauma were included. Two reviewers (SP and SV), independently screened the studies. The titles and abstracts were screened for eligible studies, whose full texts were accessed and studied thoroughly. The articles that pertained to the study aim were identified and short listed for inclusion. Any selection conflicts between the two authors were resolved by discussion with the other co-authors for final consensus. The studies were analyzed and summary of evidence generated.

Evidence to decision

The guideline panel reviewed all the information generated from the systematic reviews. The members reassessed the information and after panel discussion, gave decision regarding critical outcomes. Finally, the panel formulated recommendations and revealed its direction (for or against) and graded its strength (strong or weak).

Interpretation of recommendation

Strong Recommendation: The guideline panel is confident that the desirable effects of intervention outweigh its undesirable effects (strong recommendation for an intervention) or that the undesirable effects of an intervention outweigh its desirable effects (strong recommendation against an intervention).

Weak Recommendation: According to the guideline panel, the desirable effects probably outweigh the undesirable effects (weak recommendation for an intervention) or undesirable effects probably outweigh the desirable effects (weak recommendation against an intervention) but appreciable uncertainty exists.

Summary of guidelines

Category1: Pelvis and acetabular fractures planned to be managed conservatively; Patient Haemodynamicaly stable, no contraindications to chemical prophylaxis and no medical comorbidities

Common modalities of VTE prophylaxis available for use.

Chemical (Pharmacological)

Low Molecular Weight Heparins (LMWHs)

Unfractionated Heparin

Oral Vitamin K Antagonist Anti-Coagulants New Anticoagulant Therapies

Aspirin

Mechanical

Sequential compression devices (SCDs), Graduated compression stockings (GCSs) or Venous foot pumps (VFPs)

IVC filters

Table 2 PICO Framework for defining research questions.

Patients with Pelvi-acetabular trauma	Informal question	PICO Framework				
		Population	Intervention	Comparison	Outcome	Study design
Category-1	Is VTE prophylaxis Required?	Planned for conservative management	Any chemical agent/ Mechanical device	No chemical agent/ Mechanical device	Symptomatic/Asymptomatic DVT, Fatal/Non fatal PE, mortality	RCT/ Observational
	Preferred mode of prophylaxis	Same	Any chemical agent	Mechanical device	Same	Same
	Preferred chemical agent of prophylaxis	Same	Any chemical agent	Any chemical agent	Same	Same
	Timing of prophylaxisinitiation	Same	Within 24 h of injury	More than 24 h post injury	Same	Same
	Duration of prophylaxis	Same	Less than 1month	More than 1month	Same	Same
Category-2	Is VTE prophylaxis Required?	Planned for operative management (hemodynamically stable)	Any chemical agent/ Mechanical device	No chemical agent/ Mechanical device	Symptomatic/Asymptomatic DVT, Fatal/Non fatal PE, mortality	RCT/ Observational
	Preferred mode of prophylaxis	Same	Any chemical agent	Mechanical device	Same	Same
	Preferred chemical agent of prophylaxis	Same	Any chemical agent	Any chemical agent	Same	Same
	Timing of prophylaxisinitiation	Same	Within 24 h of injury	More than 24 h post injury	Same	Same
	Duration of prophylaxis	Same	Less than 1month	1month	Same	Same
Category 3	Is VTE prophylaxis Required?	Critically ill patient presenting to emergency department (Ongoing bleeding and high risk of Bleeding)	Any chemical agent/ Mechanical device	No chemical agent/ Mechanical device	Symptomatic/Asymptomatic DVT, Fatal/Non fatal PE, mortality	RCT/ Observational
	Preferred mode of prophylaxis	Same	Any chemical agent	Mechanical device	Same	Same
	Preferred chemical agent of prophylaxis	Same	Any chemical agent	Any chemical agent	Same	Same
	Duration of prophylaxis	Same	Less than 1month	More than 1month	Same	Same
	Do IVC filters required?	Same	Retrieveable IVC filters	No filters	Same	Same
Category 4	Is VTE treatment Required?	Patient with established DVT and planned for surgery	Any chemical agent	No chemical agent	Symptomatic/Asymptomatic DVT, Fatal/Non fatal PE, mortality	RCT/ Observational
	IVC filters required in Pre Operative period?	Same	Retrieveable IVC filters	No filters	Same	Same
Category 5	Is VTE prophylaxis Required?	Patient with medical co-morbidities	Any chemical agent/ Mechanical device	No chemical agent/ Mechanical device	Symptomatic/Asymptomatic DVT, Fatal/Non fatal PE, mortality	RCT/ Observational
Hepatic dysfunction	Preferred mode of prophylaxis	Same	Any chemical agent	Any chemical agent	Same	Same
Renal dysfunction (Cr Cl < 30)	1 1 2	Same	Any chemical agent	Any chemical agent	Same	Same
Renal dysfunction (Cr Cl < 30)	Preferred chemical agent of prophylaxis	Same	Any chemical agent	Any chemical agent	Same	Same

Table 3
Search strategy.

Database	Period: Inception to July 21, 2020	Results
PubMed	534	
(((((("venous thro	mbosis" [MeSH Terms] OR ("venous"	
[All Fields] ANI		
thrombosis" [A		
"vein" [All Field	ds]) AND "thrombosis" [All Fields])) OR	
"deep vein thro	ombosis" [All Fields]) OR (("pulmonary	
	SH Terms] OR ("pulmonary" [All Fields]	
	n" [All Fields])) OR "pulmonary	
	Fields])) OR (("venous	
	ism" [MeSH Terms] OR ("venous" [All	
	romboembolism" [All Fields])) OR	
	boembolism" [All Fields])) AND	
	oular" [All Fields] AND (((((("injuries"	
	ding] OR "injuries" [All Fields]) OR	
	ields]) OR "wounds and injuries" [MeSH	
Terms]) OR ("w	ounds" [All Fields] AND "injuries" [All	
Fields])) OR "w	ounds and injuries" [All Fields]) OR	
	Fields]) OR "traumas" [All Fields])) OR	
	ll Fields] OR "pelvis" [MeSH Terms]) OR	
	elds]) OR "pelvic" [All Fields]) AND	
	e" [All Fields] OR "injured" [All Fields])	
	MeSH Subheading]) OR "injuries" [All	
	ounds and injuries" [MeSH Terms]) OR	
	Fields] AND "injuries" [All Fields])) OR	
	njuries" [All Fields]) OR "injurious" [All	
Fields]) OR "inj	ury s" [All Fields]) OR "injured" [All	
	urys" [All Fields]) OR "injury" [All	
	("pelvics" [All Fields] OR "pelvis" [MeSH	
	lvis" [All Fields]) OR "pelvic" [All Fields])	
	actur" [All Fields] OR "fractural" [All	
	cture s" [All Fields]) OR "fractures, bone"	
	OR ("fractures" [All Fields] AND "bone"	
	R "bone fractures" [All Fields]) OR	
	Fields]) OR "fractured" [All Fields]) OR	
	Fields]) OR "fracturing" [All Fields])))	224
Embase (11)	1 1 1 1 0	221
	omboembolism'/exp OR	
	ism) AND in AND ('pelvic'/exp OR	
	ractures'/exp OR fractures)	400
Scopus	an area AND through a such aliams) (note:	409
	enous AND thromboembolism) (pelvic	
AND fractures)		

- Recommendation 1.1 For patients undergoing non operative treatment for Pelvis and acetabular fractures, the guideline panelrecommends using pharmacological prophylaxis ± mechanical.
- Prophylaxis (Grade 1D) (strong recommendation, very low evidence).
- Recommendation 1.2 For patients undergoing non operative treatment for Pelvis and acetabular fractures, the guideline panel recommends using pharmacological prophylaxis as a preferred mode of prophylaxis (Grade 1D) (strong recommendation, very low evidence).
- Recommendation 1.3 For patients undergoing non operative treatment for Pelvis and acetabular fractures, the guideline panel recommends using pharmacological prophylaxiswith LMWHas a preferred agent for prophylaxis (Grade 1D) (strong recommendation, very low evidence).
- Recommendation 1.4 For patients undergoing non operative treatment for Pelvis and acetabular fractures, the guideline panel recommends use of early prophylaxis with LMWH (within 24 h after injury). (Grade 1D) (strong recommendation, very low evidence).
- Recommendation 1.5 For patients undergoing non operative treatment for Pelvis and acetabular fractures, guideline panel recommends using extended antithrombotic prophylaxis (>1

month) over short-term antithrombotic prophylaxis (Grade 1D) (strong recommendation, very low evidence).

Conclusion

"We recommend chemical prophylaxis should be given. LMWH is the preferred choice in the patients planned for non operative management. The prophylaxis should be started within first 24 h. The duration of prophylaxis should be more 4 weeks".

Details of Summary of evidence, summary of findings, study details, certainty of evidence, evidence to decision making criteria and conclusions for Category 1 are provided in supplementary materials.

Category2: Pelvis and acetabular fractures planned for operative management; Patient Haemodynamicaly stable, no contraindications to chemical prophylaxis and no medical comorbidities

- Recommendation 2.1 For patients undergoing surgery for Pelvis and acetabular fractures, the guideline panel recommends using pharmacological prophylaxis or mechanical prophylaxis (Grade 1C) (strong recommendation, low evidence).
- Recommendation 2.2 For patients undergoing surgery for Pelvis and acetabular fractures, the guideline panel recommends using pharmacological prophylaxis as a preferred mode of prophylaxis (Grade 1C) (strong recommendation, low evidence)
- Recommendation 2.3 For patients undergoing surgery for Pelvis and acetabular fractures, the guideline panel recommends using LMWHas a preferred agent for prophylaxis (Grade 1C) (strong recommendation, low evidence)
- Recommendation 2.4 For patients undergoing surgical treatment for Pelvis and acetabular fractures, the guideline panel recommends use of early prophylaxis with LMWH (within 24 h after injury) (Grade 1B) (strong recommendation, moderate evidence)
- Recommendation 2.5 For patients undergoing operative treatment for Pelvis and acetabular fractures, guideline panel recommends using extended antithrombotic prophylaxis (>1 month) over short-term antithrombotic prophylaxis (Grade 1D) (strong recommendation, very low evidence)

Conclusion-

"We recommend early administration of prophylaxis with LMWH as soon as patient is hemodynamically stable and there is negligible risk of bleeding. The operative intervention should not be delayed beyond 2 weeks. ^{15–18} The duration of prophylaxis should be more than 4 weeks postoperatively and can be extended further if period of immobilization increases further".

Details of Summary of evidence, summary of findings, study details, certainty of evidence, evidence to decision making criteria and conclusions for Category 2 are provided in supplementary materials.

Special scenario: Delayed presentation of patients (category 1 and 2) to Hospital (more than 24 h) $-\,$

Usual practice Point-"Early initiation of prophylaxis is preferred over delayed prophylaxis; however when patients present late, it is still recommended to start prophylaxis as it is superior over not administering prophylaxis"

Category 3: Critically ill patient presenting to emergency department (Ongoing bleeding and high risk of Bleeding)

- Recommendation 3.1 For Critically ill patient patients having Pelvis and acetabular fractures, the guideline panel recommends using Immediate Mechanical prophylaxis (As patient's bleeding risk is high for initiation of pharmacological prophylaxis) (Grade 1C) (strong recommendation, low evidence)
- Recommendation 3.2 For Critically ill patient patients having Pelvis and acetabular fractures, the guideline panel recommends using pharmacological prophylaxis once the bleeding risk subsides (The risk assessment of bleeding should be done on daily basis) (Grade 1C) (strong recommendation, low evidence)
- Recommendation 3.3 For Critically ill patients having Pelvis and acetabular fractures, the guideline panel recommends using Unfractionated Heparin (UFH) as a preferred agent for prophylaxis (Grade 1D) (strong recommendation, very low evidence)
 Usual practice Point- "Evidence for the chemical agent of choice is lacking in this scenario, however as a usual practice point the panel prefers UFH as an agent as it can be monitored; and if bleeding occurs, Protamine Sulfate is an available antidote."
- Recommendation 3.4 For Critically ill patients having Pelvis and acetabular fractures, at discharge (stable patient), the guideline panel recommends using extended antithrombotic prophylaxis (>1 month) over short-term antithrombotic prophylaxis (Grade 1D) (strong recommendation, very low evidence)
 Recommendation 3.5 For Critically ill patients having Pelvis and acetabular fractures, the guideline panel recommends against the use of Prophylactic IVC filters (Grade 1B) (strong recommendation, moderate evidence)

Conclusion-

"We recommend immediate mechanical prophylaxis and daily assessment of risk of bleeding; and to start chemical prophylaxis with Unfractionated heparin (UFH) when there is minimal or no risk of bleeding. Recent evidence is against use of prophylactic IVC Filters for this patient group".

Details of Summary of evidence, summary of findings, study details, certainty of evidence, evidence to decision making criteria and conclusions for. Category 3 are provided in supplementary materials.

Category 4: Patient with established DVT and planned for surgery (Pre-Operative developed DVT)

- Recommendation 4.1 For pelvi-acetabular trauma patients with established DVT and planned for surgery, the guideline panel recommends using pharmacological treatment for DVT (Grade 1C) (strong recommendation, low evidence)
- Recommendation 4.2 For patients with established DVT and planned for surgery, the guideline panel suggests retrievable IVC filters as prophylaxis to prevent PE risk during surgery (as manipulation is a risk factor) (Grade 3D) (weak recommendation, very low evidence)
- Usual Practice point- "The VTE treatment has to be stopped 12 h before surgery and to be restarted after surgery"

Conclusion-we recommend standard pharmacological treatment of DVT and in addition use of the retrievable IVC filters for category 4 patients

Details of Summary of evidence, summary of findings, study details, certainty of evidence, evidence to decision making criteria and conclusions for Category 4 are provided in supplementary materials.

Category 5: Patient with medical co-morbidities

- Recommendation 5.1 For patients with medical co-morbidities having pelvi-acetabular fractures, the guideline panel recommends using Immediate mechanical prophylaxis (Grade 1D) (strong recommendation, very low evidence)
- Recommendation 5.2 For patients with medical co-morbidities (Hepatic Dysfunction) having pelvi-acetabular fractures, the guideline panel recommends using UFH as a preferred pharmacological prophylaxis agent (Grade 1D) (strong recommendation, very low evidence)
- Usual practice Point- "Evidence for the chemical agent of choice is lacking in this scenario, however as a usual practice point the panel prefers UFH as an agent as it can be monitored; and if bleeding occurs, Protamine Sulfate is an available antidote."
- Recommendation 5.3 For patients with medical co-morbidities (Renal dysfunction with Cr Clearance <30) having pelviacetabular fractures the guideline panel recommends using UFH as a preferred pharmacological prophylaxis agent (Grade 1D) (strong recommendation, very low evidence)
- Recommendation 5.4 For patients with medical co-morbidities (Renal dysfunction with Cr Clearance >30) having pelviacetabular fractures the guideline panel recommends using Fondaparinux as a preferred pharmacological prophylaxis agent (Grade 1C) (strong recommendation, low evidence)

Details of Summary of evidence, summary of findings, study details, certainty of evidence, evidence to decision making criteria and conclusions for Category 5 are provided in supplementary materials.

Role of newer anticoagulants

Dabigatran, rivaroxaban and apixaban are oral, reversible and directly acting anticoagulants. This new class of anticoagulants is quite convenient to the patients as there is no need of monitoring as pharmacodynamics of this class is quite predictable and there is no need of frequent dosing. The baseline renal function should be assessed. The majority of the studies demonstrating the role of newer anticoagulants have been performed in hip and knee arthroplasty, 20–23 and few in hip fractures. Patients with polytrauma or pelvic-acetabular fractures are a totally different group and very few studies have mentioned their use. Positive results from arthroplasty cannot be extrapolated and there is need for good studies to evaluate their role. There is lack of evidence demonstrating superiority of these newer agents in pelviacetabular trauma and hence there is no strong evidence to support the use of these newer agents in pelvic trauma.

Conclusion

In pelvi-acetabular fractures there is strong evidence to suggest that thromboprophylaxis should be given. It should be initiated as early as possible after control of hemorrhage. The chemical prophylaxis is the preferred mode and LMWH is the preferred agent of choice. The mechanical methods can be used as an adjunct. The routine prophylactic use of IVC filters is not recommended. However, the use of retrievable IVC filters in high risk patients with established VTE in preoperative period can be considered. The use of newer directly acting oral anticoagulants is gaining importance.

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Part of the Recommendation panel.- all 9 authors part of recommendation panel.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcot.2020.09.011.

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Conflicts of interest

None.

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