

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 45521

Title: Effectiveness of Venous Thromboembolism Prophylaxis in Patients with Liver Disease

Reviewer's code: 03261379

Reviewer's country: Romania

Science editor: Fang-Fang Ji

Date sent for review: 2019-01-10

Date reviewed: 2019-01-16

Review time: 9 Hours, 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Congratulations on your extensive work. The indications for profilactic anticoagulation are a highly debatable subject in patients with chronic liver disease especially cirrhosis. However, I have some concerns/ suggestions regarding the article: - The core tip should



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not enumerate authors but should state the central idea and result of the study. - Do you see a reasonable explanation why the group with no prophylaxis had an increase in bleeding events? - Did you take into account the localization of VTE in the decision of anticoagulation and especially type of anticoagulation? - Why did you exclude new oral anticoagulants? They are suitable for patients with liver disease (for example chronic hepatitis) without cirrhosis. - The schematic of exclusion/ inclusion criteria should be more extensive - I think your work should be completed by a prospective clinical trial assessing indications for prophylactic anticoagulation based on biologic parameters (coagulation times, serum levels proteins C and S), in order to establish a clear recommendation on anticoagulation.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [Y] No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 45521

Title: Effectiveness of Venous Thromboembolism Prophylaxis in Patients with Liver Disease

Reviewer's code: 03646970

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2019-01-18

Date reviewed: 2019-01-27

Review time: 10 Hours, 9 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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			Conflicts-of-Interest:
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			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

1. Cirrhosis was previously considered to be a hypo coagulable state and prophylaxis for VTE was felt to be unnecessary or even potentially harmful due to presumed risk of bleeding. This notion has however changed and there is a significant body of literature



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proving that cirrhotics are at risk for VTE especially PVT and that the risks of chemoprophylaxis may be outweighed by its benefits. Multiple retrospective studies have tried to answer this question however given the variations in size, methodology and populations included in these studies, firm conclusions cannot be arrived at. What this field really needs is standardized, well designed Randomized Controlled trials. Additionally, reports suggest that chemoprophylaxis may slow disease progression and fibrosis in cirrhotics and improve long term outcomes therefore this field is highly relevant.

2. Authors present a retrospective study to assess if there is a net clinical benefit of chemoprophylaxis in cirrhotic patients. Being retrospective in nature, the study is prone to certain biases. The authors perform propensity score matching between patients who did or did not receive VTE prophylaxis in order to arrive at a reliable conclusion. VTE and major bleeding were primary (and secondary) end points. Authors observed that chemoprophylaxis did not reduce risk of VTE in cirrhotic patients. Interestingly they observed that the risk of major bleeding was lower in those receiving chemoprophylaxis.

Comments

3. When talking about major bleeds, the authors list "critical sites". There is no mention of GI bleeds. What percentage of patients with bleeding had a GI bleed? What percent of these bleeds were considered to meet criteria for major bleed?

4. The decision to start someone on DVT prophylaxis is usually made by the admitting physician and patients with higher perceived risk of bleeding are usually not given prophylaxis. This can significantly skew the results during retrospective analysis.

5. Cirrhosis is a complex state with a fragile balance between the new levels of anticoagulants and procoagulants. While the study compares INR, PT and APTT they have been shown to poor predictor of VTE in cirrhotic patients. Data on genetic coagulation abnormalities for patients with VTE is not available in this study.

6. Please provide breakdown by definitions used to define incident VTE. Additionally, provide the percentages of Portal vs non-portal VTE

7. Patients presenting with Variceal



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Hemorrhage were not excluded from the study. Did anyone with variceal hemorrhage receive chemoprophylaxis? 8. It is ok to use ICD code for identification of patients with possible cirrhosis. However specific criteria should during medical record review to confirm a diagnosis of cirrhosis. What criteria did the authors use? 9. Rate of incident VTE and risk of major bleeding are primary and secondary endpoints 10. Core tip needs to be revised 11. What are the novel findings in this study?

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