**Comentários aos Revisores**

"Pharmacologic prophylaxis of venous thromboembolism in terminally ill patients: a
necessity or a waste – a clinical case."

**Notas do editor:**

Com o objectivo de optimizar a legibilidade do seu artigo e assim incrementar potencialmente as citações do mesmo, recomendamos que os conteúdos redigidos em inglês sejam revistos por um "native speaker", tradutor qualificado ou empresa especializada em serviços de "language polishing".

Os conteúdos em inglês foram revistos por um "native speaker".

**Revisor C**

1. Penso que o artigo foi apresentado de forma bastante clara e lógica e que
é de extrema importância a publicação de casos reais como este, de
decisões importantes a tomar em fases avançadas de doenças terminais,
onde o foco deve ser o doente e não a doença.

Agradecemos o comentário.

1. No entanto, acho importante clarificar que na discussão - 2º parágrafo -
há uma informação dúbia. Nos tumores do trato gastrointestinal (tumor em
questão no caso) as guidelines já defendem que até uma tromboprofilaxia
primária deve ser feita (em casos particulares) e que em casos de
tromboprofilaxia secundária (o caso apresentado) deve ser mantida até ao
final da vida e não apenas por 6 meses, sendo que em ambos as situações a
dose instituída é terapêutica e não profilática como em guidelines para
doentes não oncológicos

Agradecemos o comentário. Levámos em consideração e incluímos este facto na discussão.

1. Acho que enriqueceria o artigo clarificar as indicações para o grupo de
tumores em questão (sendo muito prevalentes na população portuguesa)
tornando esta questão ainda mais pessoal e atual na nossa prática clínica
diária e tão importante a discussão sobre quando a suspender.
Agradecemos o comentário. Levámos em consideração e incluímos este facto no texto.
2. Outro ponto, penso que alguma informação se torna excessiva na descrição
do exame objetivo, sendo uma proposta de melhoria só referir os aspetos
fora do normal e de forma mais sucinta para dar uma ideia geral do estado do
doente sem ser demasiado extenso. Um fator não referido que enriqueceria o
raciocínio clínico realizado é o peso do doente.

Agradecemos o comentário. Levámos em consideração e simplificámos o exame objectivo. Incluímos o peso que existia no processo clínico, seis dias antes da morte.

1. Mais uma vez refiro a relevância da publicação de mais artigos sobre este
tema numa revista como a Acta Médica. Cada vez mais nos deparamos com situações do género, em que vemos clínicos divididos entre a teoria das guidelines e o valor da sua aplicação na prática clínica, acabando por cair num meio termo, como o caso descrito, em que medidas são instituídas de forma errada (60 mg de

enoxaparina qd) numa tentativa de se equilibrarem entre o que ética e clinicamente parece o melhor para o doente e o que teoricamente está descrito ser o mais seguro

sem queremos

Agradecemos o comentário. Fizemos uma curta reflexão ética e moral.

1. Acho fulcral focar esta dualidade na discussão do caso uma vez que é tão
clara e que espelha muito bem o tema do artigo (“un-necessity of starting
antithrombotic therapy”). (Nota: neste caso, a profilaxia secundária, uma
vez decidida a sua instituição, teria de ser feita de forma terapêutica
com uma dose de acordo com o peso do doente distribuída de 12/12 horas no caso da enoxaparina ou um uma toma diária no caso da tinzaparina.)
Agradecemos o comentário. Levámos em consideração e incluímos este facto no texto.
2. Em termos de ranking de prioridade, penso que se enquadraria nos primeiros
10% da revista uma vez tida em conta a crítica construtiva realizada.
Muitos Parabéns aos autores por não desistir de chamar atenção para
temas muito atuais e interessantes. Cumprimentos.

Agradecemos o comentário.

**Revisor D**

I) If we are assuming gastric cancer I would suggest to share the gastric biopsy result. Is it adenocarcinoma or squamous cell or rare subtype?

It wasadenocarcinoma. We add that information into the paper.

II-1) What was gastric cancer stage at diagnosis?

It was advanced disease, stage IV. We add that information into the paper.

II-2) If it was a stage IV at diagnosis we can assume chemotherapy and radiotherapy were proposed as part as a palliative strategy?

Yes, they were used as a palliative strategy. We add that information into the paper.

II-3) Is there available data regarding chemotherapy regimens? Which agents were
used?
We know that platinum agents were used. We add that information into the paper.

II-4) It might be useful to briefly state stage and treatment intent.

We did that, as suggested.

III-1) What was patient ECOG and was the patient still on treatment when DVT was
diagnosed?

The ECOG was 2 (capable of only limited self-care, confined to bed or chair 50% or more of waking hours).

Yes, the patient was still on treatment (chemo and radiotherapy) when DVT was diagnosed.

We add that information in the paper.

III-2) Was indefinite LMWH treatment discussed with the patient/oncology/PC team?

To be honest, we do not know. The patient only stayed at the PC unit for 2 days. There was no time to get to know that information. In his clinical file there was no written mention of such a specific discussion.

We add that information into the paper.

III-3) Direct oral anticoagulants have been added as options for VTE treatment?

To be honest, we do not know. In the patient’s clinical file there was no written mention of that.

We add that information into the paper.

III-4) You could consider to include informations by the time of DVT diagnosis that could influence anticoagulation decision like 1)ECOG 2) was the disease in progression? 3) was the patient receiving chemotherapy?

Please, refer to answers II-1) and III-1).

We add that information in the paper.

IV-1) If it was a stage IV at diagnosis we can assume chemotherapy and
radiotherapy were proposed as part as a palliative strategy?

Yes, as we mentioned above.

IV-2) Discontinuation was related to suspension of all life-prolonging treatments
and/or discontinue disease-specific therapy?

We are only able to say that disease-specific therapy was discontinued.

We add that information in the paper.

In the patient’s clinical file there was no written mention to suspension of all life-prolonging treatments.

V) When were disease-specific therapy discontinued?

In October 2018. We add that information in the paper.

He was only referred to PC consultation in February 2019 (and not 2018 as we mis-wrote in the paper). We corrected that in the text.

VI) With the expression “In the last week” is hard to understand the timeline. I would suggest “x days/weeks/months before PC admission”.

We corrected it. We wrote “six days before PC unit admission”.

VII) We corrected “Omeprazole”.

VIII) We corrected “PC admission”.

IX) We corrected “cancer”.

X) Please consider including extra references, namely European guidelines and Portuguese guidelines for VTE and Cancer, as well as USA guidelines for VTE and Cancer.

We thank you a lot for having suggested that. We included that in our text (references 9,10,11 and 12).

XI) Please consider including extra references (namely USA guidelines for VTE and Cancer) and to explore further reasons not no treat.

We thank you a lot for having suggested that. We included that in our text.

XII) It could enrich the discussion to share other results of the mentioned paper. Please rephrase.

We did that in the new version of our paper.

XIII-1) It could be too much stating that the author report that thromboprophylaxis should not be performed since that authors also state that the decision should be taken individually.

We thank you a lot for having suggested that. We included that in our text.

We put Zabrocka’s paper highlights in our conclusion.

XIV) It would be advisable to rephrase “Consider pharmacological VTE prophylaxis for people who are having palliative care”……..

After your suggestion, we added that in our text.

XV-1) Please elaborate or clarify. There is no clear statement that there is sub-therapeutic levels in the references 1 and 9.

We deleted that sentence.

XV-2) On the other hand, reference (9) published data on high bleeding risk of these patients. That fact should impact decisions regarding the use of thromboprophylaxis in palliative care patients.

We inserted that in our paper.

XV-3) As well as reference (11) the majority of patients with metastatic disease remain anticoagulated up to or within days of death. Despite the limitations of retrospective data across healthcare settings, it appears that anticoagulation as death approaches confers a significant bleeding risk without additional benefit of preventing VTE symptoms

We enhanced that in our new version.

XV-4) You may consider to highlight risk of bleeding based on (9) and (11)

We did so.

XV-5) Reference (10), published more than 20 years ago states that research favours the use of LMWH rather than warfarin….

We deleted reference 10.

XVI) Consider to only consider reference 1.

We proceeded accordingly.

XVII) Please rephrase “acknowledging the fact that moral factors may interfere with medical decision is not equal to…….

We thank you a lot for having suggested that. We included that in our text.

XVIII) NICE guidelines were updated. Please refer to the latest guidelines.

We thank you a lot for having suggested that. We included that in our text.