Rapports - Vendredi 3 octobre 2014

Europe : prévention de la récidive de la maladie thrombo-embolique veineuse (MTEV) 1re partie (08h30—10h00)

RV01
Optimal duration of secondary prevention of VTE

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Treatment of venous thrombosis is aimed to prevent thrombus extension and embolization and to reduce the risk of recurrence. Recurrent venous thrombosis may occur within the first few days or weeks, but also after several months or years. This risk is, at lease in part, determined by the presence or absence of major risk factors at the time of the index event. Randomized controlled trials have shown that all patients with proximal deep vein thrombosis or pulmonary embolism benefit from a minimum of three months of anticoagulant therapy. After this period, it has been suggested that patients with an expected annual recurrence rate of less than 5% can safely discontinue treatment. These patients are those with major transient risk factors such as surgery, immobilization, trauma, pregnancy or hormonal therapy. For all other patients, including those with previous VTE, cancer or unprovoked events, this treatment duration may not be sufficiently protective and indefinite treatment duration should be considered. Because case-fatality rate for major bleeding in patients taking warfarin for more than three months is higher than case-fatality rate of recurrent venous thromboembolism, an individual patient approach to identify lower risk patients who can safely discontinue treatment at three months is warranted. Clinical prediction rules or management strategies based on D-dimer levels or residual vein thrombosis have been proposed and need further refinement and validation. Meanwhile, alternative treatment strategies with the direct oral anticoagulants or with aspirin have been proposed. The results of extended treatment studies with the direct oral anticoagulants suggest that these compounds are highly effective as compared to placebo and may reduce the risk of bleeding as compared to warfarin, while aspirin results in a less striking risk reduction when indirectly compared to any oral anticoagulant drug, but with a lower incidence of major bleeding events.

Keywords Maladie thromboembolique veineuse; Prévention secondaire

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RV01 bis
Apport de RIETE dans la durée du traitement anticoagulant

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Venous thromboembolism (VTE) carries a considerable risk of recurrence and anticoagulants should be administered for at least 3 months, but the optimal duration of treatment remains uncertain for most patients. We aimed to explore the actual duration of anticoagulant treatment in clinical practice by using the database of an international, prospective registry on patients treated for VTE, RIETE. Information was collected on baseline characteristics, risk factors for VTE and bleeding, and on therapeutic strategies. Treatment duration was censored at > 12 months and multivariate analysis using logistic regression was performed to identify predictors of treatment duration. A total of 8295 patients were enrolled; 29.9% had transient risk factors, 26.3% had cancer, and 43.7% had unprovoked VTE. Median duration of treatment was 390 days in patients with unprovoked events, 282 days in patients with transient risk factors and 181 days in cancer patients (P < 0.001). After the exclusion of patients who died during the first year of observation, the rate of patients treated for > 12 months was 62.4%, 46.8%, and 46.9%, respectively (P < 0.001). After multivariate analysis, unprovoked VTE, prior VTE, pulmonary embolism at presentation, and age > 65 years were independently associated with treatment for > 12 months; body weight < 75 kg, anemia, and occurrence of major bleeding were associated with treatment for < 12 months.

We conclude that the duration of VTE secondary prevention is heterogeneous in clinical practice and does not entirely follow current recommendations. A substantial proportion of patients with transient risk factors receives long-term anticoagulation and may be exposed to an unnecessary risk of bleeding.

Keywords Durée du traitement anticoagulant; Étude RIETE

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RV02

Does the duration of anticoagulant therapy have an influence on the prevention of venous thromboembolic disease?

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Following the landmark study by Barritt and Jordan in 1960, in which patients with venous thromboembolism (VTE) were randomized to no treatment or a combination of heparin and warfarin, antithrombotic therapy for this disease became widely accepted. This study was stopped prematurely because half of the non-treated patients had recurrent pulmonary embolism (PE), or died. It was subsequently found that after a VTE, patients given warfarin alone had a 3–4-fold higher incidence of recurrent VTE than patients given both heparin and warfarin. Since the 1990s, standard therapy for VTE has comprised an initial 5–7-day course of parenteral anticoagulant plus warfarin continued for at least 3 months. The first breakthrough was the introduction low molecular weight heparin (LMWH), which by its virtue of a fixed dose regimen given subcutaneously, allowed out of hospital treatment. The second breakthrough concerns the development of several orally active small molecules, which have been evaluated in the treatment of VTE, including a direct thrombin inhibitor and direct Factor Xa inhibitors. Other novel oral agents are also in development for VTE treatment, as well as a long-acting, reversible parenteral agent. Although the DTI ximelagatran, the first oral agent to be introduced since warfarin was withdrawn from the market in Europe because of hepatotoxicity, evidence from clinical trial evaluating other single target-specific oral agents in the treatment of VTE is convincing. It is therefore likely that use of heparin/warfarin in the treatment and secondary prevention of VTE will decrease now that these novel oral agents have been introduced for these indications. The first study in VTE with dabigatran was published in December 2009. The last large trial with edoxaban has been published in 2013. The clinical evidence from all these studies will be reviewed as well as what will be next.

Keywords Maladie thromboembolique veineuse; Durée du traitement; Anticoagulants

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RV03

La durée du traitement anticoagulant a-t-elle une influence sur la prévention de la récidive superficielle de la thrombose veineuse superficielle ?

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La question est celle de la durée optimale du traitement anticoagulant d’une thrombose veineuse superficielle (TVS), certes pour éviter une récidive mais aussi et surtout une extension de la TVS initiale ou l’apparition d’une thrombose veineuse profonde (TVP) ou d’une embolie pulmonaire (EP). La TVS est une maladie fréquente dont la bénignité est remise en cause. Il existe dans 25% des cas, même en soins primaires, une TVP et/ou une EP concomitantes et, dans les TVS isolées, une complication thromboembolique symptomatique à 3 mois dans 10% des cas. L’étude CALISTO (3002 patients), comparant en double aveugle le Fondaparinux (2,5 mg/j/45 j) à un placebo dans la TVS isolée, a montré une réduction de 79% du risque de complication thromboembolique symptomatique sans augmentation du risque hémorragique. Le risque de TVP et/ou d’EP dans le groupe placebo n’a été que de 1,3% mais les malades les plus à risque ont été exclus. Il y a eu en outre dans ce groupe 7,3% d’extensions symptomatiques de la TVS (contre 1,1% dans le groupe Fondaparinux), patients qui ont reçu dans la majorité des cas un traitement anticoagulant curatif, ce qui a certainement diminué le risque de survenue de TVP ou d’EP dans ce sous-groupe. Concernant la durée optimale du traitement anticoagulant l’étude STENOX (424 patients) a démontré qu’une durée de 10 jours était insuffisante, ce qu’a confirmé l’étude STEFLUX (635 patients). L’étude VESALIO (185 patients) a suggéré qu’un traitement anticoagulant d’un mois était insuffisant. L’étude STEFLUX a en plus montré pour les 2 groupes traités un mois, qu’il y a eu 7% de complications thromboemboliques symptomatiques dans les 2 mois suivant l’arrêt du traitement. L’étude CALISTO a par contre montré qu’après un traitement de 45 jours il n’y a eu aucun effet rebond dans le mois suivant l’arrêt du traitement (0,3% de complication thromboembolique par groupe). L’AMM européenne préconise pour la TVS un traitement de 30 et 45 jours suivant l’importance du risque thromboembolique. Dans certaines situations (grossesse, cancer évolutif) la durée optimale du traitement doit probablement être supérieure à 45 jours. À l’inverse, pour les malades à faible risque la durée de 30 jours pourrait être suffisante. Des études complémentaires sont nécessaires pour préciser les durées optimales de traitement dans ces différentes populations.

Mots clés Thrombose veineuse superficielle; Durée de traitement

Déclaration d’intérêts L’auteur n’a pas transmis de déclaration de conflits d’intérêts.

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RV04

Risk stratification and prevention of venous thromboembolic disease in cancerology

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Patients with cancer are at high risk of venous thromboembolism (VTE), which leads to significantly increased morbidity and mortality. The rates of VTE vary between 0.5% and 20% per year and depend mainly on cancer-specific and treatment-related risk factors. Also individual risk factors related to patients'characteristics contribute to occurrence of cancer-associated VTE.