Sujet 1

Extraits de l'article « Low-Molecular-Weight Heparine Versus A Coumarin For The Prevention Of Recurrent Venous Thromboembolism In Patients With Cancer » (Lee A. et al, NEJM, 2003)

Background

The standard treatment for acute venous thromboembolism consists of initial therapy with low-molecular-weight heparin or unfractionated heparin followed by long term therapy with an oral anticoagulant. This approach is highly effective in most patients, but patients with cancer have a substantial risk of recurrent thromboembolism and hemorrhagic complications. Furthermore, oral anticoagulant therapy is problematic in patients with cancer. Drug interactions, malnutrition, vomiting, and liver dysfunction can lead to unpredictable levels of anticoagulation. Secondary prophylaxis with low-molecular-weight heparin may be a more effective and practical alternative to oral anticoagulant therapy. The therapeutic dosage is based on the patient's weight, and laboratory monitoring is not routinely required. With a rapid onset of action and predictable clearance, they are also convenient for patients who require frequent interruptions of anticoagulant therapy. We performed a multicenter, randomized, open-label clinical trial to investigate whether the low-molecular-weight heparin dalteparin is more effective and safer than oral anticoagulant therapy in preventing recurrent thromboembolism in patients with cancer who have acute venous thromboembolism.

Methods

Patients with cancer who had acute, symptomatic proximal deep-vein thrombosis, pulmonary embolism, or both were randomly assigned to receive low-molecular-weight heparin (dalteparin) at a dose of 200 IU per kilogram of body weight subcutaneously once daily for five to seven days and a coumarin derivative for six months (target international normalized ratio, 2.5) or dalteparin alone for six months (200 IU per kilogram once daily for one month, followed by a daily dose of approximately 150 IU per kilogram for five months). Randomization was stratified according to the clinical center and centralized at the coordinating center (Henderson Research Centre, Hamilton, Ontario, Canada.)

The primary efficacy outcome was the first episode of objectively documented, symptomatic, recurrent deep-vein thrombosis, pulmonary embolism, or both during the six-month study period. Secondary outcome events included clinically overt bleeding (both major bleeding and any bleeding) and death.

The initial calculation of the sample size was based on an estimated risk of recurrent thrombosis of 20 percent at six months among patients treated with oral anticoagulant therapy. In order to detect a 50 percent reduction in risk with a power of 0.85 and a two-sided alpha of 0.05, it was determined that 70 primary efficacy outcome events were required. In order to adjust for the loss to follow-up from early death, the sample size was increased by 20 percent. Accordingly, we determined that 676 patients would be required.

An analysis of efficacy end points was performed according to the intention-to-treat principle and included all randomized patients who had a confirmed, qualifying thrombotic event and active cancer. The primary analysis of efficacy was based on the time from randomization to the first recurrent thromboembolic event. Data on patients without events were censored at the time of the six-month visit or death, whichever occurred first. The risk of recurrence over time was estimated according to the Kaplan–Meier method, and the treatment groups were compared with use of the two-sided log-rank test. All suspected events were reviewed by a central adjudication committee whose members were unaware of the patients' treatment assignments. Supporting documents, including clinical notes, imaging studies, and the results of laboratory tests, were forwarded to the coordinating center for adjudication.

Results

During the six-month study period, 27 of 336 patients in the dalteparin group had recurrent venous thromboembolism, as compared with 53 of 336 patients in the oral-anticoagulant group (hazard ratio, 0.48; P=0.002). The probability of recurrent thromboembolism at six months was 17 percent in the oral-anticoagulant group and 9 percent in the dalteparin group. No significant difference between the dalteparin group and the oral anticoagulant group was detected in the rate of major bleeding (6 percent and 4 percent, respectively) or any bleeding (14 percent and 19 percent, respectively). The mortality rate at six months was 39 percent in the dalteparin group and 41 percent in the oral-anticoagulant group.

Conclusions

In patients with cancer and acute venous thromboembolism, dalteparin was more effective than an oral anticoagulant in reducing the risk of recurrent thromboembolism without increasing the risk of bleeding.

Table 1. Base-Line Characteristics of the Patients.*

Characteristic	Dalteparin (N=338)	Oral Anticoagulant (N=338)
Mean age (yr)	62±12	63±13
Female sex (no. of patients)	179	169
ECOG performance score (no. of patients)		
0	80	63
1	135	150
2	118	122
3†	5	3
Hospitalization status (no. of patients)		
Outpatient	169	156
Inpatient	169	182
Hematologic cancer (no. of patients)	40	30
Solid tumor (no. of patients)		
No clinical evidence of disease	36	33
Localized disease	39	43
Metastatic disease	223	232
Antineoplastic treatment (no. of patients)‡	266	259
Current smoker (no. of patients)	33	42
History of DVT or PE (no. of patients)	39	36
Recent major surgery (no. of patients)	62	67
Central venous catheter (no. of patients)	46	40
Qualifying thrombotic event (no. of patients)		
DVT alone	235	230
PE, with or without DVT	103	108

* Plus–minus values are means ±SD. ECOG denotes Eastern Cooperative Oncology Group, DVT deep-vein thrombosis, and PE pulmonary embolism.
† Eight patients were included in the study before the protocol was amended to exclude patients with an ECOG score of 3 or 4.
‡ Antineoplastic treatment included chemotherapy, radiation, and surgery.

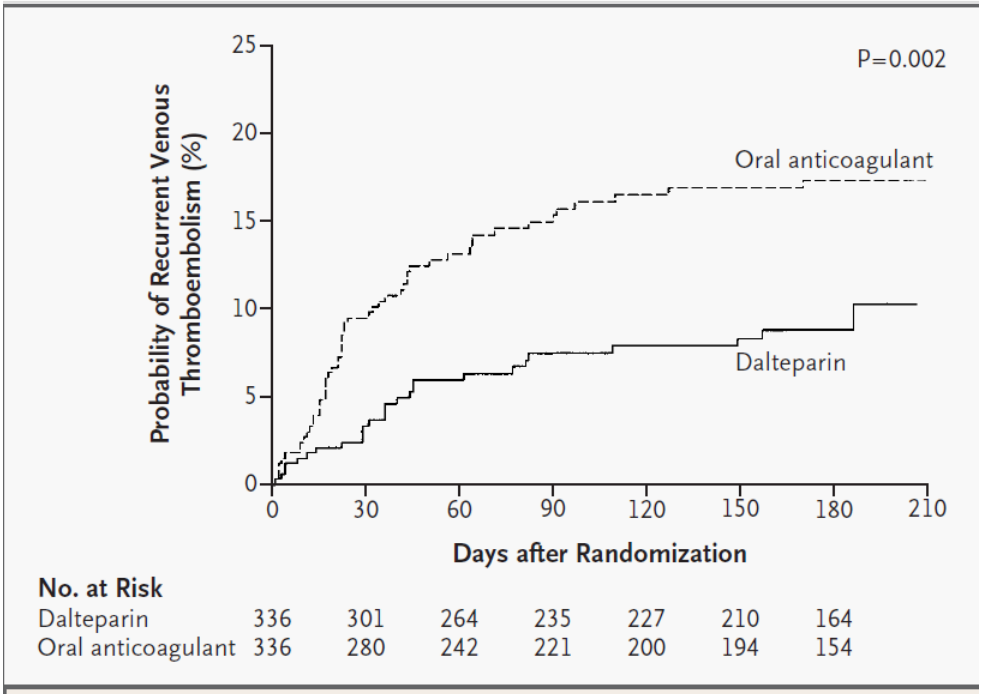

Figure 1. Kaplan–Meier Estimates of the Probability of Symptomatic Recurrent Venous Thromboembolism among Patients with Cancer, According to Whether They Received Secondary Prophylaxis with Dalteparin or Oral Anticoagulant Therapy for Acute Venous Thromboembolism.

An event was defined as an objectively verified, symptomatic episode of recurrent deep-vein thrombosis, pulmonary embolism, or both during the six-month study period. The hazard ratio for recurrent thromboembolism in the dalteparin group as compared with the oral-anticoagulant group was 0.48 (95 percent confidence interval, 0.30 to 0.77; P=0.002 by the log-rank test).

Sujet 2

Extraits de l'article « *A chapter a day : Association of book reading with longevity* » (Bavishi A. *et al*, Social science & medecine, 2016).

Background

Reading books promotes "deep reading," which is an immersive process, that promotes empathy, social perception, and emotional intelligence. These are cognitive processes that can lead to greater survival. Better health behaviors and reduced stressmay explain this process.

This study examined whether those who read books have a survival advantage over those who do not read books.

Methods

The study was conducted in the Health and Retirement Study, a US nationally representative cohort of 3635 participants who provided information about their reading patterns. Time spent reading books was assessed at baseline by the question: "How many hours did you actually spend last week reading books?".

Vital status was determined by matching participants to the National Death Index*. Follow-up time was calculated from the inclusion until either death or end datepoint (December 31, 2012). Covariates included individual comorbidities (cancer, lung disease, heart disease, stroke, arthritis, diabetes, and hypertension), visual acuity, wealth, marriage status, job status, depression, age, sex, race, selfrated health, education, and cognitive engagement.

Reading was split into three levels : T1 = 0 hours, T2 = 0.01 to 3.49, T3 = 3.5 or more hours per week. The first tertile (T1) was the reference group. Cox proportional hazards models were based on survival information up to 12 years after baseline.

Results

A dose-response survival advantage was found for book reading by tertile ($HR_{T2} = 0.83$, $p < 0.001$, $HR_{T3} = 0.77$, $p < 0.001$), after adjusting for relevant covariates including age, sex, race, education, comorbidities, self-rated health, wealth, marital status, and depression.

Conclusions

These findings suggest that the benefits of reading books include a longer life in which to read them. Our results contrast with previous studies but it may be due to our larger sample and a more detailed measure of reading compared with other studies.

* Le national death index est un registre national des décès

HR= Hazard Ratio, s'interprète globalement comme un Risque Relatif (RR)