Concomitant VTE increased risks for mortality and hemorrhage in older patients with cancer, with risk varying by cancer type

Gross CP, Galusha DH, Krumholz HM. **The impact of venous thromboembolism on risk of death or hemorrhage in older cancer patients.** J Gen Intern Med. 2007;22:321-6.

Clinical impact ratings: Hematol/Thrombo ★★★★★☆☆ Oncology ★★★★★★☆

QUESTIONS

In older patients with a first diagnosis of cancer, how frequently is venous thromboembolism (VTE) diagnosed concomitantly? Does VTE increase risks for 1-year mortality and major hemorrhage?

METHODS

Design: Inception cohort followed for 1 year.
Setting: United States.
Patients: 167 385 patients ≥ 67 years of age (median age 75 y, 52% men, 87% white) who were diagnosed with 1 of 10 cancer types (prostate, breast, bladder, uterus, lung, colorectal, lymphoma, pancreas, kidney, or ovary), had a malignant primary lesion with a known month of cancer diagnosis, and did not have a diagnosis of VTE 6 to 24 months before cancer diagnosis. Exclusion criteria included date of death before cancer diagnosis, ineligibility for Medicare Part A or B, and enrollment in a managed care plan within 2 years before cancer diagnosis.
Prognostic factors: Concomitant VTE (diagnosis between 6 mo before and 1 mo after cancer diagnosis), age, race, sex, cancer stage, histologic grade, chemotherapy, radiation, cancer-specific surgery, comorbid conditions, and socioeconomic status (SES).
Outcomes: Mortality and major hemorrhage (intracranial or gastrointestinal hemorrhage requiring hospital admission).

MAIN RESULTS

1.1% of patients had concomitant VTE. Concomitant VTE increased the risk for 1-year mortality for 8 of 10 cancer types (all but prostate and breast) (Table). Major hemorrhage occurred more frequently in patients with concomitant VTE than in those without VTE, both overall and for 8 of 10 cancer types (all but kidney and uterine) (Table).

CONCLUSIONS

In older patients with a first diagnosis of cancer, 1.1% had a concomitant diagnosis of venous thromboembolism (VTE). Concomitant VTE increased risks for 1-year mortality and major hemorrhage, with risk varying by cancer type.

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For correspondence: Dr. C.P. Gross, Yale University School of Medicine, New Haven, CT, USA. E-mail: cary.gross@yale.edu.

Mortality and major hemorrhage at 1 year in older patients with a first diagnosis of cancer and concomitant VTE*

Cancer type	Number of patients	Hazard ratio (95% CI) for mortality associated with VTE†	Major hemorrhage rates		Excess hemorrhage rate in VTE patients (*P* value)
			With concomitant VTE	Without concomitant VTE	
Breast	26 563	1.01 (0.77 to 1.33)‡	10%	3.1%	6.9% (0.004)
Lung	32 348	1.16 (1.05 to 1.27)	13%	8.1%	4.5% (0.003)
Colorectal	29 101	1.19 (1.06 to 1.34)	26%	18%	7.9% (< 0.001)
Prostate	40 710	1.21 (0.96 to 1.52)‡	8.5%	3.6%	4.9% (0.007)
Pancreas	6393	1.26 (1.06 to 1.49)	24%	16%	7.9% (0.02)
Ovary	3359	1.32 (1.03 to 1.68)	15%	8.0%	6.6% (0.033)
Bladder	11 063	1.43 (1.13 to 1.80)	13%	5.3%	7.9% (0.001)
Kidney	4141	1.43 (1.13 to 1.80)	11%	8.4%	2.1% (0.45)‡
Lymphoma	8022	1.63 (1.35 to 1.97)	22%	11%	12% (< 0.001)
Uterus	5685	1.96 (1.47 to 2.62)	1.9%	4.4%	–2.5% (0.36)‡
Total	167 385		17%	7.9%	8.9% (< 0.001)

*VTE = venous thromboembolism; other abbreviations defined in Glossary. RRR, RRI, and CI calculated from data in article.
†Adjusted for age, sex, race, cancer characteristics, cancer treatments, comorbid conditions, and socioeconomic status.
‡Not significant.

COMMENTARY

Clinicians have likened decisions about anticoagulation to walking a tightrope—a misstep to one side increases the risk for bleeding and a misstep to the other increases the risk for thrombosis.

The study by Gross and colleagues emphasizes how often the fall into bleeding occurs. This well-done inception cohort study clarifies several key issues about older patients with VTE and cancer. It confirms that concomitant VTE is an ominous prognostic marker in older patients with some types of cancer and clarifies the mechanism for this observation.

Prognosis worsens when VTE accompanies cancer types usually detected at an advanced stage (e.g., pancreas) but not those detected at an early stage (e.g., breast or prostate). Similarly, patients with VTE and certain types of cancer had higher rates of major bleeding, although bleeding did not appear to be the cause of death. Therefore, it seems that the contribution of VTE to cancer mortality relates most to the stage of the underlying malignancy when VTE is diagnosed, rather than to VTE or its treatment. The study also highlights the high background risk for major bleeding (7.9%) in older patients with cancer, even in the absence of anticoagulants. This suggests that certain types of cancer should be risk factors in prediction tools for bleeding risk.

Some limitations bear note. As pharmacy data were not available, there was probably some contamination of the groups (i.e., it is not assured that all VTE patients received anticoagulants or that all non-VTE patients did not). However, the authors' correction for other common indications for anticoagulation mitigates this problem. Quality of warfarin management also could not be ascertained. Data were obtained before publication of guidelines (1) that suggest use of prolonged low-molecular-weight heparin products in lieu of warfarin. The impact of this recommendation on bleeding rates in older cancer patients therefore could not be addressed.

Much work remains to be done. Although we know that the risk for both thrombosis and hemorrhage is higher in older cancer patients than in patients without cancer, we still lack clear guidance on balancing these risks. At present, the results of Gross and colleagues' study should lead clinicians to carefully consider the risks and benefits of anticoagulants in patients with VTE receiving palliation for advanced cancer.

Scott M. Stevens, MD
C. Gregory Elliott, MD
LDS Hospital and the University of Utah
Salt Lake City, USA

Reference

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