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The Burden of Hospital Readmissions for Venous Thromboembolism Among Patients With Cancer

PRESENTER

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During the American Society of Hematology's Annual Meeting in December 2018, real-world data were presented showing the significant burden of hospital readmissions for venous thromboembolism (VTE) among individuals with cancer. Alpesh N. Amin, MD, MBA, lead investigator of the study, discussed the findings and their relevance, highlighting the need for more investigation and the implementation of measures to manage patients at risk for VTE with in-hospital and postdischarge prophylaxis. Following is a summary of the study results.

Patients with cancer or who have a history of cancer are at an increased risk of developing venous thromboembolism (VTE) events, which often manifest as deep vein thromboses or pulmonary embolisms (PEs).¹ Data suggest that appropriate thromboprophylaxis in these patients is both challenging and underutilized.² Patients who are not receiving appropriate thromboprophylaxis are at risk for developing VTE events, which may require rehospitalization. The clinical and economic burden of VTE-related hospital readmissions among these patients is not well understood in the real-world setting.

OBJECTIVES AND METHODS

To analyze the frequency and associated cost of VTE-related hospital readmissions among patients with cancer in the United States, investigators compared a population of patients who were hospitalized for acute medical illnesses, including heart failure, respiratory diseases, ischemic stroke, cancer, infectious diseases, and rheumatic disease (N = 12,785), with a subpopulation of patients hospitalized for cancer (n = 2002).³ Patients were identified from the MarketScan database, which captures discharge diagnosis codes, between July 1, 2011, to March 31, 2015. The first hospitalization was classified as the index hospitalization. Patients were required to have 6 months of continuous insurance coverage at the baseline period and during the follow-up period of the index hospitalization event, allowing for 1 year of continuous data.

Outcome measurements included: (1) proportion of patients readmitted for VTE-related or primary VTE discharge diagnosis, (2) time to VTE readmission from discharge, and (3) associated costs of readmissions for patients with a primary discharge diagnosis of VTE.

RESULTS

Patients hospitalized for cancer were younger than all acute medically ill patients. Among acute medically ill patients, 44% were <65 years compared with 62% in the cancer population. Other baseline

Table. Baseline Demographics

Parameter	All Patients (N = 12,785)	Patients Hospitalized for Cancer (n = 2002)
Mean age (SD), years	68.3 [13.7]	63.4 [11.8]
Female, n (%)	6591 (51.5)	983 (49.1)
Geographic region		
South	8459 (66.2)	1424 (71.1)
North Central	2391 (18.7)	310 (15.5)
West	1210 (9.5)	158 (7.9)
Northeast	713 (5.6)	109 (5.4)
Charlson Comorbidity Index score		
Mean	3.1 (2.6)	5.1 (3.2)
Median	2	4

demographics are shown in the **Table**. Off all patients hospitalized for acute medical illness, 15.7% were hospitalized for cancer. Mean length of hospital stay (5.2 days) was the same for all patients compared with patients hospitalized for cancer.

Rates of readmission for any VTE during the 6-month follow-up period were higher among patients hospitalized with cancer (3.9%; 51.3% of these readmissions were for primary VTE) compared with all acute medically ill patients (2.1%; 36.6% of these readmissions were for primary VTE).

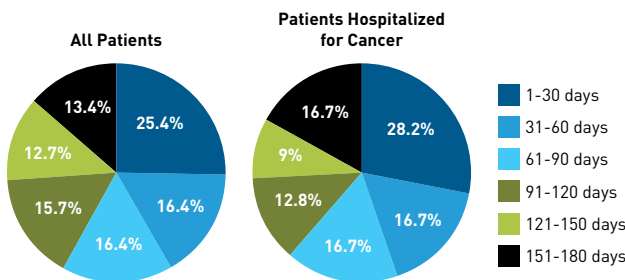
As shown in **Figure 1**, over one quarter of the patients were readmitted for VTE within 30 days of discharge (28.2% of patients with cancer vs 25.4% of all acute medically ill patients). The mean length of stay associated

with VTE-related hospital readmissions was 7.6 days for primary VTE for patients initially hospitalized for cancer compared with 9.4 days for all acute medically ill patients. The mean length of stay associated with readmission for primary VTE was 5.2 days for patients with cancer and 5 days for acutely ill patients.

As shown in **Figure 2**, costs associated with VTE-related readmissions were \$35,102 for patients with cancer versus \$42,158 for all acute medically ill. For primary VTE-related events, the mean costs for rehospitalization were \$19,961 vs \$18,681, respectively.

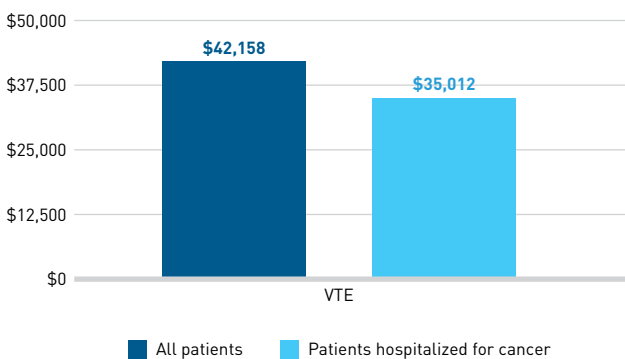
Potential limitations of this study are related to the MarketScan database, which can generate errors resulting from erroneous coding entry or the database itself. Additionally, the database may not be reflective of the United States population because the majority of MarketScan claims are in the South Census region, abiding by that region's standard of care, compared with other regions of the United States. Nevertheless, MarketScan is generally considered to have a healthy amount of data.

Figure 1. Time to VTE Readmission



VTE indicates venous thromboembolism.

Figure 2. Burden of VTE-Related Hospital Readmissions



VTE indicates venous thromboembolism.

CONCLUSIONS

With over 30% of cancer patients being readmitted for VTE within 30 days postdischarge, the results of this real-world study suggest that prophylaxis is underutilized in this population in the United States. Moreover, the economic burden of VTE readmissions for patients with cancer, as well as for patients with other acute medical illnesses, is significant. •

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ASK THE PRESENTER: A Q&A WITH ALPESH N. AMIN, MD, MBA



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Could you talk about the overall value that can be gained from a real-world study such as this?

Real-world vs randomized controlled studies are complimentary in nature. A randomized controlled trial is prospective in design and it offers prespecified outcomes, whereas a real-world study is generally observational—retrospective in design. There is more of an association [to be seen with real-world studies] as opposed to cause-and-effect [outcomes with randomized controlled trials], but real-world studies do tell you how things perform in the real clinical practice. Real-world results also allow people to look for research questions and gaps in care; they [can] find opportunities to fix, treat, or improve practice design and outcomes. In this type of real-world epidemiological study, we identify that there are gaps in care and that venous thromboembolism [VTE] occurs across a continuum. A significant number of hospital readmissions come from the cancer population, and that raises the question about how to manage these patients who are leaving the hospital and are at risk for readmissions—which comes with significant cost and burden to the healthcare system.

Why do you feel the patients with acute medical illnesses, specifically cancer, are not receiving appropriate thromboprophylaxis?

Four clinical trials—MAGELLAN, APEX, ADOPT, and EXCLAIM—have shown that there is likely value in giving prophylaxis for about 30 days to the at-risk medical population, to improve the outcome of recurring VTE. Maybe the supposition is that patients are in the hospital for a shorter period now compared with previous trials that came out years ago, [which has] taught us that we should offer prophylaxis to patients in the hospital for the prevention of VTE. At that time, the length of hospital stay for patents was a lot longer. Now, we have decreased the length of stay significantly, and patients do not need to be in the hospital for that long. But just because they are not in the hospital that long, does not mean they don't have an increased risk of VTE. To manage these patients, maybe we need to give thromboprophylaxis in the high-risk population when they leave the hospital. This has not been studied well in the cancer population, which is generally considered a higher risk population for VTE. Our study showed some important findings, such as how many patients have VTE after leaving the hospital. We also wanted to ask the question: What was the readmission risk for these patients for developing

VTE? [Our findings show that] readmission for getting VTE was quite significant in the cancer population. This raises future opportunities for practitioners to think about prophylaxis [beyond discharge], which could possibly reduce the risk of VTE readmissions and the clinical and economic burden associated with it.

With many of the newer anticoagulants, the risk of getting a bleed is significantly lower than previous anticoagulants, and the dosage is generally smaller for prophylaxis compared with treatment dosages. I think there is merit for looking into how one should manage the cancer patients in terms of VTE across the continuum, which would require additional studies. We decided to look at the impact on cancer vs other at-risk medically ill patients including cancer. It was cancer against the total medically at-risk ill population, and you can see [that] the cancer patients had more of a significant issue than the rest of the entire population, when you combine it together.

Based on your findings, what can you hypothesize about future directions in research? Do you think continued research will increase awareness for the importance of prophylaxis?

VTE is the third leading cause of cardiovascular mortality, and we know that it is a significant healthcare burden as well as cost burden. We also know that there is opportunity and that cancer is only growing

“With many of the newer anticoagulants, the risk of getting a bleed is significantly lower than previous anticoagulants and the dosage is generally smaller for prophylaxis compared with treatment dosages.”

in the population. As incidence of cancer continues to grow, so does the risk for VTE. As we continue to see more patients in the ambulatory setting, we must be able to manage across the continuum in a safe and effective manner. We know that readmissions are a big burden to the healthcare delivery system; it is an outcome measure used by CMS. Tying it all together, [the issue of whether there is risk is] a very important question. This study identified that there is significant risk, leading to the next question: Do specific types of

oral anticoagulants give us a greater opportunity to manage these patients? Oral anticoagulants have less risk of bleeding [compared with older options, like warfarin] and generally better efficacy in reducing the risk of VTE in postdischarge period. One could design the trial to study this question to minimize the risk of readmission and cost burden of VTE. That is the ultimate hope.

But before you can get there, you want to define that there is a problem, and I think this real world epidemiological study demonstrates that there is a problem. Now we can take it to the next step.

What measures, if any, can be implemented to help reduce readmissions and extend out the prophylaxis to reduce those at risk?

First, we need to be able to prove that there is an intervention that can be done effectively and appropriately. Science needs to be done and proven. There should be a study in the cancer population that [investigates the following questions]: [Suppose] a patient comes in with an underlying diagnosis of cancer, and maybe also other medical or surgical issues. If one gives them prophylaxis for VTE, and continues prophylaxis for a certain period of time post discharge, can this reduce the risk of VTE? Can this reduce the risk of

readmission? Can this be done safely and effectively, and ultimately have that lead to less morbidity, less mortality, and less cost overall to the healthcare system? If the answers are yes, then it should be a practice that we do just like we do any other preventive measure that improves outcomes.

The second thing is that there needs to be a cultural acceptance [of] the supporting. Any time you do this, you are really balancing risk and benefit. If the benefit outweighs the risk, it does not mean that there is not going to be some risk. There is a risk of bleeding with anticoagulant therapy, but most bleedings can be stopped, and the worst bleedings are extremely rare. On the other hand, patients can die from a VTE or get post-thrombotic syndrome. Certainly, there are many other downstream challenges, problems, and concerns regarding VTEs that might potentially be avoidable with a lower dose anticoagulant. Additionally, many tend to not see the impact of something that is preventive versus something that needs immediate fixing. Other cultural issues include implementation within the healthcare system; that is complex and has its own barriers of implementation. Therefore, it will become important that a process that enables patients to get appropriate prophylaxis is designed and implemented with minimal barriers to care delivery. •