Percutaneous Coronary Intervention and Outcomes in Patients With Lymphoma in the United States (Nationwide Inpatient Sample [NIS] Analysis)

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Characteristics and outcomes of patients with lymphoma undergoing percutaneous coronary intervention (PCI) are unknown. Therefore, we analyzed clinical characteristics and outcomes in patients that underwent PCI and had a concomitant diagnosis of Hodgkin's (HL) or non-Hodgkin's (NHL) lymphoma. We analyzed patients with and without lymphoma diagnosis from the Nationwide Inpatient Sample in the United States who underwent PCI procedure during 2004 to 2014. Multivariable regression analysis was performed to examine the association between lymphoma diagnosis and clinical outcomes post-PCI including short-term complications and in-hospital mortality. A total of 7,119,539 PCI procedures were included in the analysis and 18,052 patients had a diagnosis of lymphoma (0.25%). These patients were likely to experience in-hospital mortality (odds ratio [OR] 1.39, 95% confidence interval [CI] 1.25 to 1.54), stroke or transient ischemic attack (OR 1.75, 95% CI 1.61 to 1.90), and any in-hospital complication (OR 1.31, 95% CI 1.25 to 1.37), following PCI. In the lymphoma subtype-analysis, diagnosis of HL was associated with an increased odds of in-hospital death (OR 1.40, 95% CI 1.24 to 1.56), any in-hospital complication (OR 1.31, 95% CI 1.25 to 1.38), bleeding complications (OR 1.12 95% CI 1.05 to 1.20), and vascular complications (OR 1.13 95% CI 1.06 to 1.20) whereas these odds were not significantly associated with non-Hodgkin's diagnosis. Finally, both types of lymphoma were associated with increased odds of stroke/transient ischemic attack following PCI (OR 1.82, 95% CI 1.67 to 1.99 and OR 1.31, 95% CI 1.05 to 1.63, respectively). In conclusion, while the prevalence of lymphoma in the observed PCI cohort was low, a diagnosis of lymphoma was associated with an adverse prognosis following PCI, primarily in patients with the HL diagnosis. **(Am J Cardiol 2019;124:1190−1197)**

Cardiovascular disease and cancer constitute 2 leading causes of death worldwide and it is expected that their prevalence and coexistence will further increase due to the aging population and shared risk factors.[1−3] Percutaneous coronary intervention (PCI) is the commonest form of revascularization in patients with coronary artery disease (CAD), with increasingly complex and multimorbid patients who underwent these procedures.[2] In contrast, lymphomas are one of the most common hematologic malignancies accounting for about 3% to 4% of all cancers worldwide with cancer registries ranking it as the second commonest hematologic malignancy.[4−6] Patients with lymphoma have an increased risk of fatal cardiovascular events compared with the general population[7] and can develop severe CAD[8] often enhanced by radiotherapy and chemotherapeutic treatment.[9] Although patients with lymphoma are at increased risk of developing CAD which is more complex and extensive, there have been no previous studies reporting on the outcomes following PCI in patients with concomitant hematologic malignancies such as lymphoma. The aim of the present study was to report on clinical and procedural characteristics and outcomes of patients with a confirmed diagnosis of Hodgkin's (HL) or non-Hodgkin's lymphoma (NHL) and to compare them to patients without lymphoma, in a nationwide contemporary cohort.

Methods

The data was obtained from the Nationwide Inpatient Sample (NIS) for hospital discharges in the United States during the period of 2004 to 2014. The NIS is the largest publicly available all-payer inpatient health care database in the United States that was developed for the Healthcare

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Cost and Utilization Project through Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality. The NIS approximates 20-percent stratified sample of all discharges from US community hospitals and due to its multistate nature is estimated to represent more than 97% of the US population.[10]

All patients aged 18 or older that had a confirmed discharge record of performed PCI during the index hospitalization between January 2004 and December 2014 were initially included in the analysis. To identify all eligible discharge records that underwent PCI from the NIS dataset we used respective International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes. Discharge codes that were captured are presented in Supplementary Table 1A.

Patient sociodemographic variables were recorded for each hospital discharge and included information about age, gender, race and ethnicity, length of stay (LOS), admission type (elective or emergent), admission day (weekday or weekend), median ZIP household income, expected primary payer, total hospitalization charge in US$, and Charlson Comorbidity Index. Since the total bill charged by the hospital does not correspond to the actual payer-end cost, these charges were multiplied by the conversion ratio in order to approximate actual final cost for the payer. Each discharge record also contained diagnosis codes for patient's diagnoses established during the index hospitalization such as ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and cardiogenic shock. Finally, patient co-morbidities and medical history items in terms of cardiovascular and cerebrovascular events were retrieved from the aforementioned diagnosis codes assigned to each discharge and were recorded as well.

Procedural PCI variables were identified by using respective procedure codes and included information on the type of vessel revascularization (single vessel or multivessel PCI) and whether PCI of the bifurcation lesion was performed. Additionally, data on the use of left ventricular assist devices or intra-aortic balloon pump (IABP), diagnostic procedures (such as the use of intracoronary pressure wire or intravascular ultrasound), and type of stent implanted (DES, drug-eluting stent or BMS, bare-metal stent) were recorded.

Patients with current lymphoma diagnoses on record were identified by using respective ICD-9 codes (Supplementary Table 1B). Main clinical outcomes of interest in this study were in-hospital mortality and complications associated with the PCI procedure. These complications included bleeding, vascular complications, cardiac complications, and postprocedural stroke or transient ischemic attack (TIA). Events of interest were captured by using patient safety indicators and ICD-9-CM codes (Supplementary Table 1C).

All data analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM, Armonk, New York) and STATA 14.0 (StataCorp, College Station, Texas). Continuous variables were presented as median and interquartile range or mean ± standard deviation (SD) where appropriate. Categorical variables were presented as number and/or percentage. Discharge cases that had greater than 10% missing data for included outcomes and covariates were removed from the analysis while random missing of data was assumed. For data analysis, sampling weights were applied, as provided by the NIS design. Due to the complexity and longitudinal nature of NIS database and changes in sampling and weighting strategies over time, recommendations from Agency for Healthcare Research and Quality to apply weights at discharge were followed since this procedure reduces the margin of error for estimates and delivers more stable estimates.

Multivariable logistic regression analysis was undertaken to examine the association between the cases with a diagnosis of lymphoma, irrespective if Hodgkin's or non-Hodgkin's, compared with cases without lymphoma on designated clinical end points including in-hospital mortality, specified complications and the composite outcome of aggregated complications. In the secondary regression analysis, separate associations of 2 main subtypes of lymphoma (HL and NHL) and in-hospital mortality and complications were examined and compared with patients without lymphoma. To account for potential confounders, all regression models were adjusted for age, gender, median income, expected payer, elective admission, weekend admission, primary diagnosis of MI, STEMI/NSTEMI, diagnosis of cardiogenic shock, use of an assisting device or IABP, stent type, multivessel PCI, bifurcation stenting, fractional-flow reserve use, intravascular ultrasound use, hospitalization year, Charlson Comorbidity Index, smoking, diabetes mellitus, hypercholesterolemia, arterial hypertension, atrial fibrillation, and previous CAD, MI, PCI, coronary artery bypass grafting or stroke/TIA. Finally, a propensity score-matched (PSM) analysis was performed in order to match respective cohorts (lymphoma vs no lymphoma patients and HL vs NHL patients) in terms of age, sex, and baseline factors and for this nearest-neighbor matching algorithm was used with caliper size of 0.2. Rates of short-term complications and in-hospital mortality were then compared between respective groups that were adjusted for PSM coefficient.

Results

A total of 7,119,539 hospital discharges from 2004 to 2014 were identified with PCI performed during the index hospitalization. Discharge cases that had greater than 10% missing data for included outcomes and covariates such as age, gender, elective procedure indication, LOS, and median income according to ZIP code, were excluded from the analysis, as shown in Figure 1. In total, about 0.61% (N = 43,917) of the original dataset was removed due to missing data whereas 76.4% of these removed records were due to missing median ZIP code income data. Excluded patients did not significantly differ from those included in any of the measured outcomes and in most of baseline characteristics (Supplementary Table 1D). Crude comparison of women and men with lymphoma diagnosis undergoing PCI in respect to short-term complications and in-hospital mortality is provided in Supplementary Table 1E. The average prevalence of patients with a diagnosis of lymphoma that underwent PCI, during the observed 10-year period, was 0.25%. Furthermore, there seems to be an increasing trend (significant at $p < 0.001$) of PCI utilization in lymphoma patients during the studied NIS period (Figure 2).

Baseline sociodemographic, clinical, and procedural characteristics of patients with lymphoma and patients

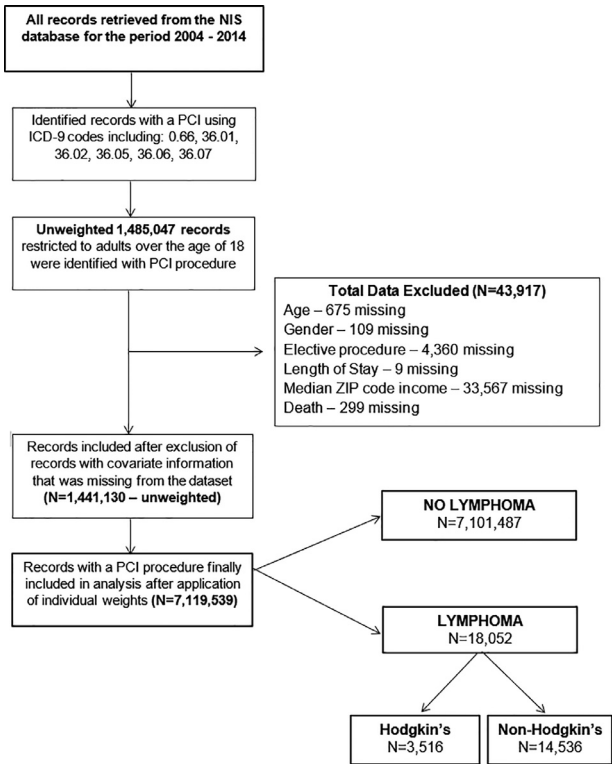

Figure 1. A study flow diagram showing inclusion and exclusion criteria and the final number of records included in the analysis.

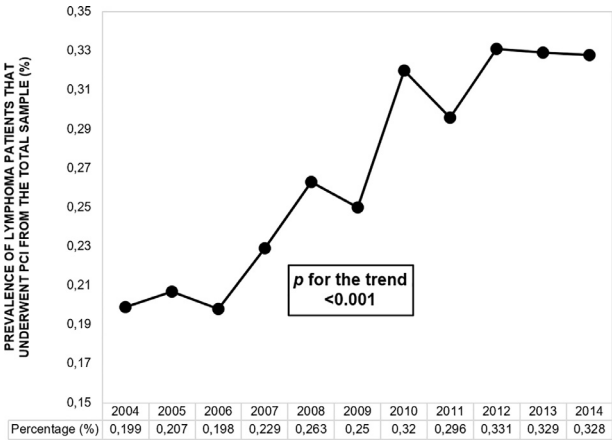

Figure 2. Trends in prevalence of lymphoma patients that underwent PCI among all patients that received PCI (data from the National Inpatient Sample during 2004−2014 period).

without lymphoma that underwent PCI are presented in Table 1. Patients with lymphoma tended to be older, of White Caucasian race, and were less likely to be admitted for an elective PCI procedure compared to nonlymphoma patients. A proportion of cases in which Medicare was designated as a primary expected payer were significantly higher in lymphoma patients than those without lymphoma. Furthermore, lymphoma patients were significantly more co-morbid, tended to stay longer in hospital, and were charged more per hospitalization compared to nonlymphoma patients. Lymphoma patients also more commonly presented with NSTEMI during index hospitalization and had a higher incidence of cardiogenic shock compared with those without lymphoma. A previous history of CAD, acute MI, coronary artery bypass grafting, and PCI was generally less prevalent in patients with lymphoma than those without, and this was also the case for traditional cardiovascular risk factors such as hypercholesterolemia, smoking, arterial hypertension, and uncomplicated diabetes mellitus.

Regarding PCI procedural characteristics, lymphoma patients were more likely to undergo multivessel revascularization with BMS implantation, accompanied with more frequent intracoronary pressure wire and/or intravascular ultrasound procedures. Similarly, LV assist devices or IABP were more likely to be used during PCI procedure in lymphoma patients which corresponds to a higher prevalence of cardiogenic shock in lymphoma patients. Regarding the lymphoma type, NHL patients were more likely to be older, have higher co-morbidity burden, a longer median LOS, and higher cost of hospitalization compared to patients with HL. Furthermore, patients with NHL were more likely to present with NSTEMI, be admitted over a weekend, and undergo multivessel coronary revascularization, bifurcation stenting, and BMS implantation with more frequent use of intracoronary pressure wire during PCI compared with HL patients. In contrast, HL patients were more likely to present with STEMI, undergo DES implantation, and suffer a cardiogenic shock at presentation, accompanied with more frequent use of LV assist device or IABP (Table 1).

Patients with a current diagnosis of lymphoma had significantly higher rates of complications and in-hospital mortality after PCI, compared with patients without lymphoma. This difference was most prominent for bleeding and vascular complications which were more than twice more common in patients with lymphoma than those without. Furthermore, NHL patients had significantly higher rates of bleeding, vascular complications, composite of complications, and postprocedural stroke/TIA, compared with HL patients who underwent PCI. The rate of cardiac complications following PCI and in-hospital mortality was similar between both types of lymphoma (Table 2). Depiction of complication and in-hospital mortality rates in patients with HL, NHL, and patients without lymphoma is provided in Figure 3.

Furthermore, in the multivariable regression model adjusted for multiple covariates, a diagnosis of lymphoma was independently associated with a significantly increased odds of bleeding (odds ratio [OR] 1.12, 95% confidence interval [CI] 1.06 to 1.19), vascular complications (OR 1.11, 95% CI 1.05 to 1.18), and composite of complications (OR 1.31, 95% CI 1.25 to 1.37) following PCI, compared with patients without lymphoma set as a reference, because this effect was not significant in the case of cardiac complications (Table 3). Finally, a diagnosis of lymphoma was associated with a significant 39% increase in odds of in-hospital death (OR 1.39 95% CI 1.25 to 1.54) and a 75% increase in odds of postprocedural stroke or TIA (OR 1.75, 95% CI 1.61 to 1.90) following PCI, compared with nonlymphoma patients.

Furthermore, when stratified by lymphoma type, diagnosis of HL was independently associated with a 40% increase in odds of in-hospital mortality, 82% increase in odds of postprocedural stroke/TIA, 12% increase in odds of

Table 1
Baseline characteristics of PCI cohort stratified by lymphoma diagnosis

Variable	No lymphoma diagnosis (N = 7,101,487)	Hodgkin's lymphoma (N = 3,516)	Non-Hodgkin's lymphoma (N = 14,536)	p-Value*	p-Value†
Age at index admission, years [IQR]	65 [56,74]	55 [48-65]	71 [62-79]	<0.001	<0.001
Charlson comorbidity index (mean ± SD)	1.07 ± 1.25	2.98 ± 1.29	3.22 ± 1.42	<0.001	<0.001
Median length of stay, days [IQR]	2 [1-4]	2 [1-4]	3 [2-5]	<0.001	<0.001
Median total charge, US$ [IQR]	15724 [11867-21426]	17078 [12350-24268]	17975 [13261-25407]	<0.001	<0.001
Men	66.3%	68.4%	66.9%	0.105	0.014
Ethnicity				<0.001	<0.001
White	79.0%	83.8%	86.9%		
Black	8.0%	6.4%	4.8%		
Hispanic	6.8%	3.9%	4.2%		
Asian/Pacific Islander	2.2%	1.6%	1.5%		
Native American	0.5%	0.0%	0.2%		
Other	3.6%	4.3%	2.4%		
Household Income				<0.001	<0.001
1st quartile	26.6%	20.7%	21.9%		
2nd quartile	26.8%	22.4%	24.6%		
3rd quartile	24.6%	24.7%	26.0%		
4th quartile	22.0%	32.3%	27.4%		
Paying modality				<0.001	<0.001
Medicare-primary payer	51.3%	34.6%	68.0%		
Medicaid-primary payer	5.7%	6.2%	3.9%		
Private insurance-primary payer	34.8%	53.5%	24.6%		
Self-pay	4.9%	2.8%	1.4%		
No charge	0.5%	0.4%	0.2%		
Other	2.8%	2.6%	1.8%		
Admission type, nonelective	72.6%	76.9%	77.2%	0.550	<0.001
Admission day, weekday	16.0%	16.5%	18.0%	0.045	<0.001
Single coronary vessel revascularization	73.3%	71.9%	71.3%	0.496	<0.001
Multivessel coronary revascularization	17.8%	19.3%	19.9%	0.336	<0.001
Bifurcation stenting	1.7%	1.3%	1.6%	0.133	0.092
Use of left ventricular assist device or intra-aortic balloon pump	3.3%	6.6%	4.8%	<0.001	<0.001
Cardiogenic shock at presentation	2.8%	4.8%	3.7%	0.001	<0.001
ST-elevation myocardial infarction	21.3%	22.8%	19.4%	<0.001	<0.001
Non-ST-elevation myocardial infarction	22.9%	26.3%	29.3%	<0.001	<0.001
Fractional flow reserve pressure wire used during percutaneous coronary intervention	0.7%	0.7%	1.3%	0.004	<0.001
Intravascular ultrasound used during percutaneous coronary intervention	4.8%	7.6%	6.2%	0.005	<0.001
Bare-metal stent implanted	28.3%	30.9%	38.6%	<0.001	<0.001
Drug-eluting stent implanted	73.2%	70.3%	62.9%	<0.001	<0.001
History of coronary artery disease	94.6%	93.4%	92.3%	0.025	<0.001
History of percutaneous coronary intervention	18.7%	20.3%	16.9%	<0.001	<0.001
History of coronary artery bypass grafting	7.3%	7.4%	6.8%	0.238	0.017
History of myocardial infarction	13.2%	13.9%	12.1%	0.005	0.006
History of cerebrovascular incident	3.8%	3.5%	4.2%	0.053	0.005
Acquired immune deficiency syndrome	0.1%	1.0%	0.6%	0.012	<0.001
Alcohol abuse	2.0%	1.9%	1.1%	0.002	<0.001
Smoker	35.2%	31.4%	27.0%	<0.001	<0.001
Rheumatoid arthritis/collagen vascular disease	1.8%	1.4%	2.9%	<0.001	<0.001
Congestive heart failure	1.0%	1.7%	2.2%	0.088	<0.001
Chronic obstructive pulmonary disease	15.5%	15.0%	17.6%	<0.001	<0.001
Diabetes mellitus, uncomplicated	33.2%	23.4%	29.6%	<0.001	<0.001
Arterial hypertension	69.6%	54.7%	64.2%	<0.001	<0.001
Atrial fibrillation	10.0%	7.7%	16.1%	<0.001	<0.001
Hypercholesterolemia‡	65.9%	59.2%	58.4%	0.358	<0.001
Obesity§	12.2%	9.6%	8.4%	0.020	<0.001
Renal failure	9.6%	7.4%	13.9%	<0.001	<0.001
Liver disease	0.9%	1.5%	0.9%	0.006	0.004
Peripheral vascular disorders	10.4%	7.2%	10.5%	<0.001	<0.001
Paralysis	0.7%	1.0%	0.7%	0.076	0.209

(*continued*)

Table 1 (*Continued*)

Variable	No lymphoma diagnosis (N = 7,101,487)	Hodgkin's lymphoma (N = 3,516)	Non-Hodgkin's lymphoma (N = 14,536)	p-Value*	p-Value†
Dementia	1.4%	0.6%	1.2%	0.001	0.001
History of leukemia	0.3%	1.2%	1.4%	0.238	<0.001
History of solid tumor without metastasis	1.2%	1.5%	2.7%	<0.001	<0.001

* Comparison of Hodgkin's vs Non-Hodgkin's lymphoma group;
† Comparison of No lymphoma vs. Lymphoma group
‡ Increased plasma concentration of cholesterol carried in low-density lipoproteins (LDL) and/or increased total cholesterol in plasma
§ Defined as body mass index ≥30 kg/m^2

Table 2
Complications and in-hospital mortality stratified by lymphoma diagnosis

Variable	No lymphoma diagnosis (N = 7,101,487)	Hodgkin's lymphoma (N = 3,516)	Non-Hodgkin's lymphoma (N = 14,536)	p Value*	p Value†
Bleeding complication	3.0%	5.0%	7.7%	<0.001	<0.001
Vascular complications	3.3%	5.8%	7.8%	0.001	<0.001
Cardiac complications	2.4%	2.6%	3.0%	0.098	<0.001
Postprocedural stroke/TIA	3.0%	2.8%	3.6%	0.031	<0.001
Any complication	8.1%	10.1%	13.5%	<0.001	<0.001
In-hospital mortality	1.6%	2.1%	2.7%	0.096	<0.001

* Comparison of Hodgkin's vs Non-Hodgkin's Lymphoma group.
† Comparison of no lymphoma vs lymphoma group.

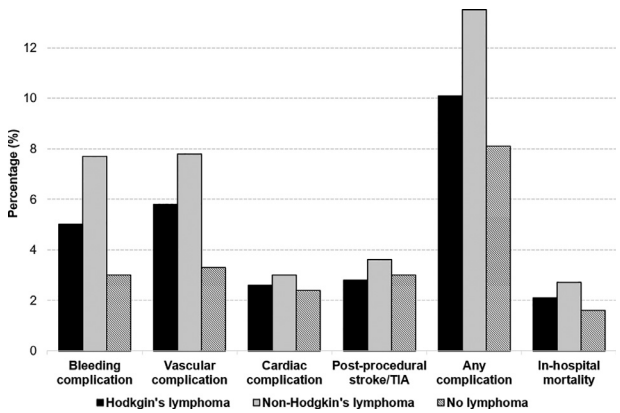

Figure 3. Percentage (%) of procedural complications and in-hospital mortality events among PCI patients stratified by a lymphoma diagnosis.

bleeding, 13% increase in odds of vascular complications, and, finally, 31% increase in the likelihood of any complication, when compared with no-lymphoma diagnosis. In contrast, no significant association was observed between NHL diagnosis and any short-term complication except for postprocedural stroke/TIA (Table 3). Multivariate-adjusted OR for each of measured outcomes in respect to lymphoma type is summarized in Figure 4.

When adjusted for propensity score, comparator analysis confirmed that HL patients had significantly higher rates of bleeding and vascular complications than NHL patients, as well as postprocedural stroke/TIA and any complications while both groups did not differ in terms of in-hospital mortality and cardiac complications (Table 4). Similarly, PSM analysis confirmed that lymphoma patients had significantly more short-term adverse events and higher in-hospital mortality compared with patients without lymphoma (Table 5).

Discussion

Our analysis of over 7 million PCI procedures, suggests that lymphoma diagnosis is independently associated with an increased odds of adverse short-term clinical outcomes, higher rates of bleeding, vascular complications, and in-hospital mortality. This was mainly limited to patients with HL once adjustments for differences in baseline characteristics were applied. No comparable studies, to our knowledge, have reported on clinical outcomes in lymphoma patients who underwent PCI.

A recent study published by our group reported that approximately to one in ten patients who underwent PCI in the United States until 2014 had a current or a previous history of cancer, but there is paucity of published data specifically in patients with lymphoma.[2] Hematologic malignancies drive thromboembolic disease through multiple procoagulant, fibrinolytic, and proteolytic factors and by activating inflammatory pathways, whereas these pathophysiologic effects are further enhanced by irradiation, chemotherapy, and immunomodulatory agents that are routinely used to treat these conditions.[11,12] The thrombotic risk in lymphomas is substantially higher in adult patients with NHL compared with those with HL, especially in advanced stages of disease for which more aggressive therapeutic strategies are employed whereas this risk is also partially driven by the typically older age of NHL patients.[13,14]

In our analyzed cohort, patients with NHL were significantly older compared with both HL patients and those without lymphoma with a greater co-morbidity burden, higher proportion of PCI procedures for acute coronary syndrome indications, more multivessel PCI, a worse cardiovascular risk factor profile, and more likely to have diabetes and renal failure. Moreover, patients with NHL had a substantially higher prevalence of atrial fibrillation that may suggest more

Table 3
Odds ratios* and 95% confidence intervals and level of significance (p value) for outcomes and in-hospital mortality of lymphoma patients compared to patients without lymphoma

Variable	Lymphoma vs no-lymphoma	p Value	Hodgkin's lymphoma vs no-lymphoma	p Value	Non-Hodgkin's lymphoma vs no-lymphoma	p Value
Bleeding complication	1.12 (1.06-1.19)	<0.001	1.12 (1.05-1.20)	<0.001	0.99 (0.84-1.18)	0.461
Vascular complications	1.11 (1.05-1.18)	<0.001	1.13 (1.06-1.20)	0.001	1.09 (0.92-1.28)	0.134
Cardiac complications	1.07 (0.98-1.17)	0.128	1.06 (0.96-1.17)	0.190	0.91 (0.72-1.16)	0.288
Post-procedural stroke/TIA	1.75 (1.61-1.90)	<0.001	1.82 (1.67-1.99)	<0.001	1.31 (1.05-1.63)	0.014
Any complication	1.31 (1.25-1.37)	<0.001	1.31 (1.25-1.38)	<0.001	1.01 (0.89-1.14)	0.601
In-hospital mortality	1.39 (1.25-1.54)	<0.001	1.40 (1.24-1.56)	<0.001	1.03 (0.77-1.38)	0.442

* Multivariable regression model was adjusted for age, sex, median income, expected payer, elective admission, weekend admission, primary diagnosis of MI, STEMI/NSTEMI diagnosis, diagnosis of shock, use of an assist device or IABP, the type of stent used, multivessel PCI, bifurcation stenting, fractional flow reserve, intravascular ultrasound, year of hospitalisation, Charlson Comorbidity Index, smoking status, hypercholesterolemia, arterial hypertension, atrial fibrillation, diabetes mellitus, history of coronary artery disease, myocardial infarction, percutaneous coronary intervention, stroke, and coronary artery bypass grafting

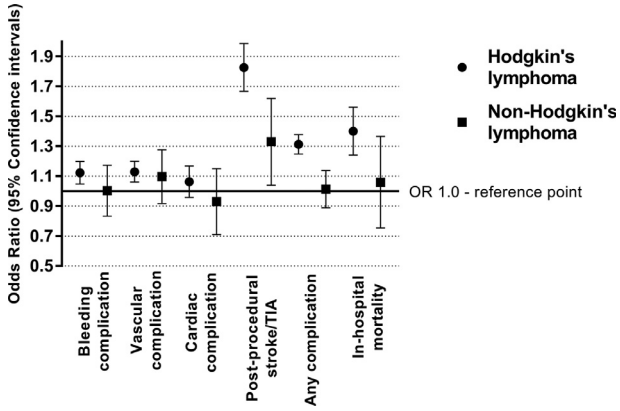

Figure 4. Multivariable-adjusted odds ratios and 95% confidence intervals for procedural outcomes and in-hospital mortality among patients that underwent PCI with Hodgkin's and non-Hodgkin's lymphoma diagnosis compared with patients without lymphoma that were set as a reference.

Table 4
Propensity score-matched* comparison of Hodgkin's and non-Hodgkin's lymphoma patients in respect to short-term complications and in-hospital mortality

Variable	Hodgkin's lymphoma (N = 2,718)	Non-Hodgkin's lymphoma (N = 2,704)	p Value*
Bleeding complication	6.0%	4.7%	0.028
Vascular complications	6.8%	4.9%	0.002
Cardiac complications	2.2%	2.7%	0.054
Postprocedural stroke/TIA	3.3%	1.6%	<0.001
Any complication	11.6%	9.6%	0.035
In-hospital mortality	1.6%	1.8%	0.656

* Propensity score-matched analysis used exact matching on age while additional covariates in the model were sex, Charlson Comorbidity Index, day of admission, nonelective procedure, median household income, obesity, smoking, arterial hypertension, hypercholesterolemia, diabetes mellitus, atrial fibrillation, chronic pulmonary disease, congestive heart failure, renal failure, multivessel disease, bifurcation lesion, cardiogenic shock, ST-elevation myocardial infarction, drug-eluting stent use, and previous history of coronary artery disease, percutaneous coronary intervention, myocardial infarction, cerebrovascular incident, and coronary artery bypass grafting. Caliper length was set at 0.2.

widespread use of anticoagulation agents. All these factors might have predisposed patients to more bleeding events, but also to more thrombotic complications and finally, short-term death following PCI. Once the higher risk profile of patients with NHL was adjusted for differences in baseline covariates, NHL was no longer associated with increased odds of in-hospital mortality or short-term complications.

In contrast, our associations with adverse outcomes and a concomitant diagnosis of HL persisted even when differences in baseline risk factor profile were adjusted for. Patients with hematologic malignancies such as those with HL are predisposed to increased risks of thrombosis, however, 95% of these complications occur during treatment, hence it is difficult to ascertain whether the prothrombotic effect is induced by the ongoing treatment or the lymphoma itself.[13] The average incidence of thrombosis in lymphoma patients is 6%, with more advanced stages of the disease incrementally increasing the risk of thrombosis, both in HL and in NHL, while there also seems to be an effect of certain chemotherapeutics affecting this risk.[13–15] Patients with hematologic malignancies such as those with HL are also prone to bleeding complications due to cell dyscrasia, alterations in platelet function and thrombocytopenia, clotting factor deficiencies, defects in vascular integrity,[16] and use of anticoagulant agents.[17,18] Both HL and NHL diagnosis were associated with increased odds of stroke/TIA following PCI although this OR was more prominent in HL patients. In the HL population, irradiation to the neck and mediastinum was the most important risk factor for ischemic stroke and TIA.[19] Given that intensive radiotherapy regimens were historically used in HL patients it could be that cerebrovascular events have been partially driven by generally higher irradiation burden in HL patients, compared with those with NHL.

Presented results suggest that interventional cardiologists should liaise with oncologists and hematologists and adopt a multidisciplinary approach in managing these complex groups of patients, for example, by establishing cardio-oncology clinics or consults.[20,21] Patients deemed to be at increased risk of major bleeding could be treated with DES platforms that only require abbreviated dual antiplatelet therapy, and judicious use of intravascular imaging to reduce the risk of stent thrombosis.[22] Radial access should be the default access site used where possible, to minimize access site-related major bleeding complications.[23–25] Antiplatelet regimes should be individualized to balance the risk of

Table 5
Propensity score-matched* comparison of patients without and with lymphoma in respect to short-term complications and in-hospital mortality

Variable	No lymphoma (N = 3,588)	Lymphoma (N = 3,588)	p Value*
Bleeding complication	7.2%	8.4%	<0.001
Vascular complications	5.1%	7.2%	<0.001
Cardiac complications	2.8%	3.8%	<0.001
Postprocedural stroke/TIA	2.1%	3.5%	<0.001
Any complication	9.8%	12.8%	<0.001
In-hospital mortality	2.6%	3.6%	<0.001

* Propensity score-matched analysis used exact matching on age while additional covariates in the model were sex, Charlson Comorbidity Index, day of admission, nonelective procedure, median household income, obesity, smoking, arterial hypertension, hypercholesterolemia, diabetes mellitus, atrial fibrillation, chronic pulmonary disease, congestive heart failure, renal failure, multivessel disease, bifurcation lesion, cardiogenic shock, ST-elevation myocardial infarction, drug-eluting stent use, and previous history of coronary artery disease, percutaneous coronary intervention, myocardial infarction, cerebrovascular incident and coronary artery bypass grafting. Caliper length was set at 0.2.

ischemic and major bleeding complications in close discussion with both hematologists and cardio-oncologists as advocated by relevant cardiovascular societies.[26–28]

There are several limitations to our study. This is a large registry-based study with all inherent limits of such study design and an impossibility to ascertain causal effects between variables. Underreporting and coding errors might be a source of bias in our analysis. Furthermore, data on disease duration, complete blood count, coagulation parameters, current or past treatments, stage/grade of lymphoma, history of radiation therapy and radiation dose, as well as the use of chemotherapeutics, antiplatelet, and anticoagulation agents were not captured in the database and these variables may contribute to the outcomes that we report. Even more, a diagnosis of NHL in this study was comprised of heterogeneous NHL cancer subtypes that vary greatly with respect to their biology and prognosis, therefore, might have a different impact on end points of interest.

In conclusion, this study shows that patients with lymphoma are more likely to sustain complications and in-hospital death following PCI. These increased odds appear to be mainly observed in HL patients, although the odds of cerebrovascular events are significantly increased in both lymphoma types. There is a paucity of studies in this patient population and findings from this study provide important data which can better inform patients, caregivers, and their treating physicians. These findings should encourage cardiologists to pursue care in close collaboration with the oncologists in order to improve outcomes.

Disclosures

The investigators have no conflicts of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.07.015.

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