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

Josip A. Borovac MD BSc, Chun Shing Kwok MBBS MSc BSc, Cezar Iliescu MD, Hun Ju Lee MD, Peter Y. Kim MD, Nicolas L. Palaskas MD, Azfar Zaman BSc MB ChB, Robert Butler MB ChB, Juan C. Lopez-Mattei MD, Mamas A. Mamas BM BCh DPhil

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Percutaneous Coronary Intervention and Outcomes in Patients with Lymphoma in the United States (Nationwide Inpatient Sample [NIS] analysis).

Josip A. Borovac MD BSc <sup>a,b,c</sup>, Chun Shing Kwok MBBS MSc BSc <sup>a,d</sup>, Cezar Iliescu MD <sup>e</sup>, Hun Ju Lee MD <sup>f</sup>, Peter Y. Kim MD <sup>e</sup>, Nicolas L. Palaskas MD <sup>e</sup>, Azfar Zaman BSc MB ChB <sup>g</sup>, Robert Butler MB ChB <sup>d</sup>, Juan C. Lopez-Mattei MD <sup>e</sup> & Mamas A. Mamas BM BCh DPhil <sup>a,d,\*</sup>

Running head title: PCI Outcomes in Lymphoma Patients

### **Author affiliations:**

<sup>a</sup>Keele Cardiovascular Research Group, Centre for Prognosis Research, Institute of Primary Care and Health Sciences, Keele University, UK, <sup>b</sup>Department of Pathophysiology, University of Split School of Medicine and University Hospital of Split, Split, Croatia, <sup>c</sup>Institute of Emergency Medicine of Split-Dalmatia County (ZHM SDZ), Split, Croatia, <sup>d</sup>Department of Cardiology, Royal Stoke Hospital, University Hospital North Midlands, Stoke-on-Trent, UK, <sup>e</sup>Department of Cardiology, Division of Internal Medicine University of Texas MD Anderson Cancer Center, Houston, TX, USA, <sup>f</sup>Department of Lymphoma & Myeloma, Division of Cancer Medicine, University of Texas MD Anderson Cancer Center, Houston, TX, USA, <sup>g</sup>Department of Cardiology, Freeman Hospital and Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK

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\*Corresponding author: Professor Mamas A. Mamas, Keele Cardiovascular Research Group, Keele University, Stoke-on-Trent ST4 7QB, United Kingdom; e-mail: mamasmamas1@yahoo.co.uk; Phone/fax: +44 (0) 1782 732933

#### **ABSTRACT**

Characteristics and outcomes of patients with lymphoma undergoing PCI are unknown. Therefore, we analyzed clinical characteristics and outcomes in patients that underwent percutaneous coronary intervention (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 US who underwent PCI procedure during 2004-2014. Multivariable regression analysis was performed to examine the association between lymphoma diagnosis and clinical outcomes post-PCI including shortterm 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 (OR 1.39, 95%CI 1.25-1.54), stroke or transient ischemic attack (TIA) (OR 1.75, 95%CI 1.61-1.90), and any in-hospital complication (OR 1.31, 95%CI 1.25-1.37), following PCI. In the lymphoma subtypeanalysis, diagnosis of HL was associated with an increased odds of in-hospital death (OR 1.40, 95% CI 1.24-1.56), any in-hospital complication (OR 1.31, 95% CI 1.25-1.38), bleeding complications (OR 1.12 95% CI 1.05-1.20) and vascular complications (OR 1.13 95%CI 1.06-1.20) while these odds were not significantly associated with NHL diagnosis. Finally, both types of lymphoma were associated with an increased odds of stroke/TIA following PCI (OR 1.82, 95% CI 1.67-1.99 and OR 1.31, 95% CI 1.05-1.63, 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.

Key words: Lymphoma; Coronary Artery Disease; Complications; Mortality

### Introduction

Cardiovascular disease and cancer constitute two 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.<sup>1-3</sup> Percutaneous coronary intervention (PCI) is the commonest form of revascularization in patients with coronary artery disease (CAD), with increasingly complex and multi-morbid patients undergoing these procedures.<sup>2</sup> On the other hand, lymphomas are one of the most common hematological malignancies accounting for about 3% to 4% of all cancers worldwide with cancer registries ranking it as the second commonest hematological malignancy. 4-6 Patients with lymphoma have an increased risk of fatal cardiovascular events compared to the general population<sup>7</sup> and can develop severe CAD<sup>8</sup> often enhanced by radiotherapy and chemotherapeutic treatment. Whilst 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 (US) during the period of 2004-2014. The NIS is the largest publicly available all-payer inpatient health care database in the US that was developed for the Healthcare Cost and Utilization Project (HCUP) through Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS approximates 20-percent stratified sample of all discharges from US community hospitals

and due to its multi-state nature is estimated to represent more than 97% of the US population. <sup>10</sup>

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 (CCI). 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 comorbidities 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 multi-vessel PCI) and whether PCI of the bifurcation lesion was performed. Additionally, data on the use of left ventricular assist devices (LVAD) 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 post-procedural 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, NY, USA) and STATA 14.0 (StataCorp, College Station, Texas, USA). Continuous variables were presented as median and interquartile range (IQR) 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 AHRQ 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 to cases without lymphoma on designated clinical endpoints including in-hospital mortality, specified complications and the composite outcome of aggregated complications. In the secondary regression analysis, separate associations of two main subtypes of lymphoma (HL and NHL) and in-hospital mortality and complications were examined and

compared to 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, multi-vessel PCI, bifurcation stenting, fractional-flow reserve use, intravascular ultrasound use, hospitalization year, CCI, smoking, diabetes mellitus, hypercholesterolemia, arterial hypertension, atrial fibrillation, and previous CAD, MI, PCI, coronary artery bypass grafting (CABG) or stroke/transient ischemic attack (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, length of stay, 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 while 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 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 non-lymphoma patients. A proportion of cases in which Medicare was designated as a primary expected payer was significantly higher in lymphoma patients than those without lymphoma. Furthermore, lymphoma patients were significantly more comorbid, tended to stay longer in hospital, and were charged more per hospitalization compared to non-lymphoma patients. Lymphoma patients also more commonly presented with NSTEMI during index hospitalization and had a higher incidence of cardiogenic shock compared to those without lymphoma. A previous history of CAD, AMI, CABG, and PCI was generally less prevalent among patients with lymphoma than those without, and this was also the case for traditional cardiovascular risk factors such as hypercholesterolemia, smoking, afterial 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 among lymphoma patients. Regarding the lymphoma type, NHL patients were more likely to be older, have higher comorbidity 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 to 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 to patients without lymphoma. This difference was most prominent for bleeding and vascular complications which were more than twice more common among patients with lymphoma than those without. Furthermore, NHL patients had significantly higher rates of bleeding, vascular complications, composite of complications, and post-procedural stroke/TIA, compared to HL patients undergoing PCI. The rate of cardiac complications following PCI and in-hospital mortality were similar between both types of lymphoma (**Table 2**). Depiction of complication and in-hospital mortality rates among 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 (OR 1.12, 95% CI 1.06-1.19), vascular complications (OR 1.11, 95% CI 1.05-1.18) and composite of complications (OR 1.31, 95% CI 1.25-1.37) following PCI, compared to patients without lymphoma set as a reference, while 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 1.25-1.54) and a 75% increase in odds of post-procedural stroke or TIA (OR 1.75, 95% CI 1.61-1.90) following PCI, compared to non-lymphoma 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 post-

procedural stroke/TIA, 12% increase in odds of bleeding, 13% increase in odds of vascular complications, and, finally, 31% increase in the likelihood of any complication, when compared to no-lymphoma diagnosis. In contrast, no significant association was observed between NHL diagnosis and any short-term complication except for post-procedural stroke/TIA (**Table 3**). Multivariate-adjusted odds ratios for each of measured outcomes in respect to lymphoma type are 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 post-procedural 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 to 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 among lymphoma patients undergoing 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 prior history of cancer, but there is paucity of published data specifically in patients with lymphoma.<sup>2</sup> Hematologic malignancies drive thromboembolic disease through multiple procoagulant, fibrinolytic and proteolytic factors and by activating inflammatory pathways, while these pathophysiological effects are further enhanced by irradiation, chemotherapy and

immunomodulatory agents that are routinely used to treat these conditions.<sup>11,12</sup> The thrombotic risk in lymphomas is substantially higher in adult patients with NHL compared to those with HL, especially in advanced stages of disease for which more aggressive therapeutic strategies are employed while this risk is also partially driven by the typically older age of NHL patients.<sup>13,14</sup>

In our analyzed cohort, patients with NHL were significantly older compared to both HL patients and those without lymphoma with a greater comorbidity burden, higher proportion of PCI procedures for ACS 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 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 an 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 hematological 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.<sup>13</sup> The average incidence of thrombosis among 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.<sup>13-15</sup> 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<sup>16</sup>, and use of anticoagulant agents.<sup>17,18</sup> Both HL and NHL diagnosis were associated with an increased odds of stroke/TIA following PCI although this odds ratio was more prominent among HL patients. In the HL population, irradiation to the neck and mediastinum was the most important risk factor for ischemic stroke and TIA.<sup>19</sup> 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 among HL patients, compared to those with NHL.

Presented results suggest that interventional cardiologists should liaise with oncologists and hematologists and adopt a multi-disciplinary approach in managing these complex groups of patients, for example, by establishing cardio-oncology clinics or consults. <sup>20,21</sup> 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. <sup>22</sup> Radial access should be the default access site used where possible, to minimize access site-related major bleeding complications. <sup>23-25</sup> Antiplatelet regimes should be individualized to balance the risk of ischemic and major bleeding complications in close discussion with both hematologists and cardio-oncologists as advocated by relevant cardiovascular societies. <sup>26,27,28</sup>

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 endpoints 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.

## **Conflict of Interest**

The investigators have no conflicts of interest to declare.

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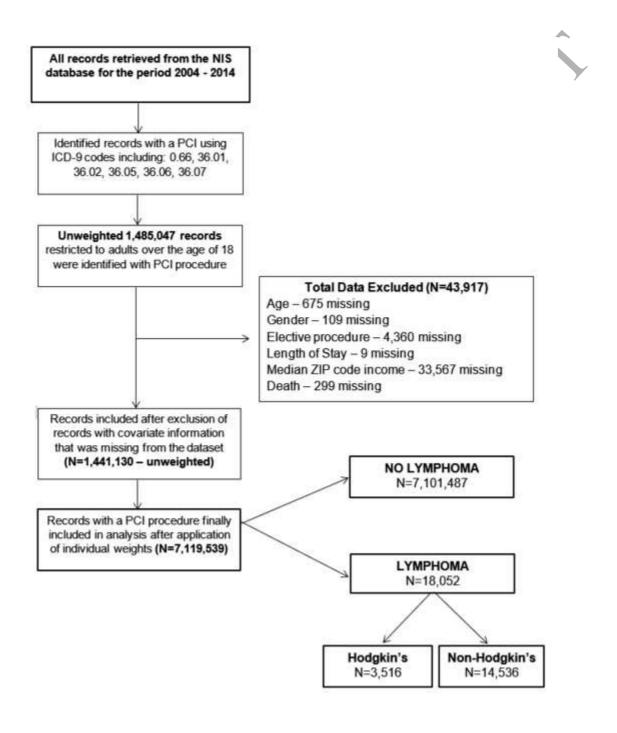
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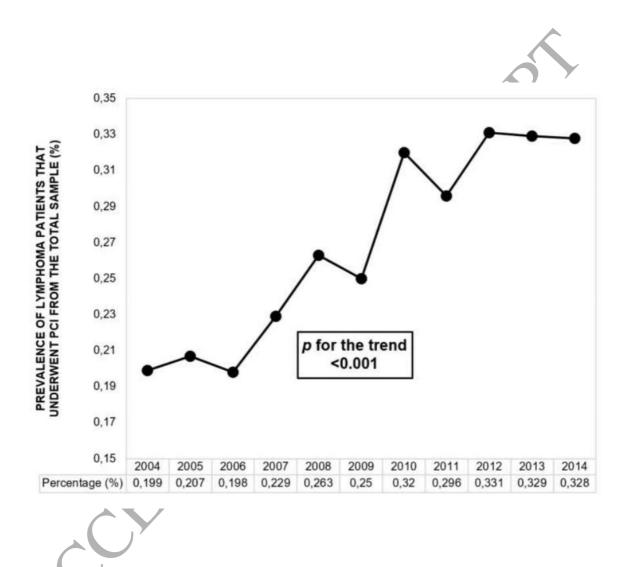
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#### FIGURE LEGENDS

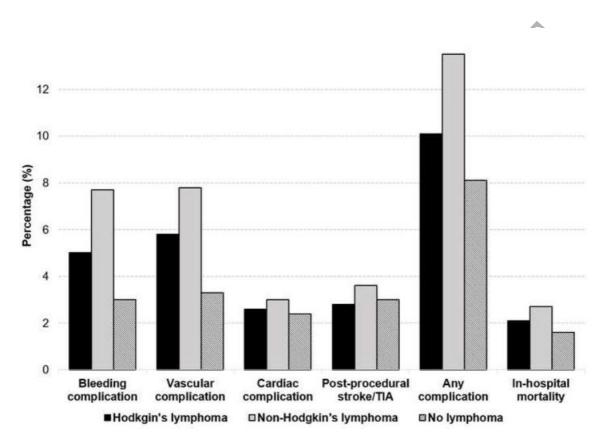
**Figure 1.** A study flow diagram showing inclusion and exclusion criteria and the final number of records included in the analysis.



**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).



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





**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 to patients without lymphoma that were set as a reference.

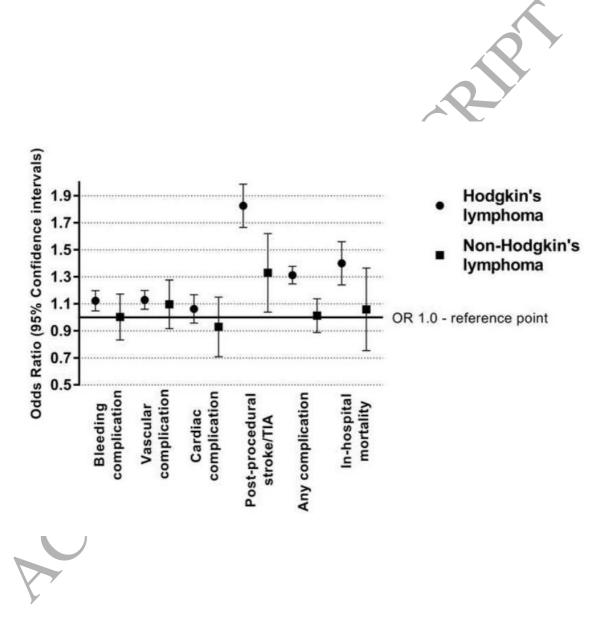


Table 1. Baseline characteristics of PCI cohort stratified by lymphoma diagnosis

No	** * * * * * * * * * * * * * * * * * * *	**	** 1 1	<b>.</b>		
diagnosis (N=7,101,487)         (N=3,516)         Lymphoma (N=14,536)           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 ± 4.42         <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, USS   15724 [11867- 17078   17975   <0.001         <0.001         <0.001         <0.001           [IQR]   21426  12350- 13261- 24268  25407          <0.001         <0.001         <0.001         <0.001           Men   66.3%   68.4%   66.9%   0.105   0.104         <0.001         <0.001         <0.001         <0.001           White   79.0%   83.8%   86.9%   86.9%   86.9%          <0.001   0.001         <0.001         <0.001           White   79.0%   83.8%   86.9%	Variable	No	Hodgkin's	Non-	<b>p</b> -	p-
Age at index admission, years [IQR] Charlson Comorbidity 1.07 ± 1.25 2.98 ± 1.29 3.22 ± 1.42 <0.001 <0.001   Index (mean ± SD) Median length of stay, days [IQR] Median total charge, US\$ 15724 [11867- 17078 17975 <0.001 <0.001   I[QR] 21426] 12350 [13261- 24268] 25407] Men 66.3% 68.4% 66.9% 0.105 0.014   Ethnicity			• •	e e	value*	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		Ö	(N=3,516)	-		
Vears   Tokan   Vears   Tokan   Vears   Tokan   Vears   Tokan   Vears   Tokan   Vears   Tokan   Vears   Vear		(N=7,101,487)		(N=14,536)		
Vears   Total   Vears   Total   Vears   Total   Vears   Total   Vears   Total   Vears   Total   Vears   Vears   Total   Vears   Vear	A	C5 [5C 74]	55 [40 <i>C</i> 5]	71 [62 70]	-0.001	ر ۱
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		03 [30,74]	33 [48-03]	/1 [02-79]	<0.001	<0.001
Index (mean ± SD)   Median length of stay, days [IQR]   2 [1-4]   3 [2-5]   <0.001   <0.001	-	1.07 + 1.25	2.09 + 1.20	2 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\$         15724 [11867- 24268]         17975         <0.001	•	$1.07 \pm 1.23$	$2.98 \pm 1.29$	$3.22 \pm 1.42$	<0.001	<0.001
Median total charge, US\$   15724 [11867-   17078   17975   20.001   20.001   [IQR]   21426]   [12350-   24268]   25407]		2.51.41	2.51.43	(2.12.51	ر ۱۸ ۸۸ ۸۸	ر ۱
Median total charge, US\$         15724 [11867- 21426]         17078 [12350- 13261- 24268]         17975 25407]         <0.001 <0.001           IQR]         21426]         [12350- 24268]         25407]	=	2 [1-4]	2 [1-4]	3 [2-5]	<0.001	<0.001
Total   Tota		15704 [11067	17079	17075	<0.001	<0.001
Men   66.3%   68.4%   66.9%   0.105   0.014     Ethnicity	<b>O</b> ,	=			<0.001	<0.001
Men         66.3%         68.4%         66.9%         0.105         0.014           Ethnicity          <0.001	[IQK]	21420]				
Ethnicity         <0.001         <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	Man	66.20/			0.105	0.014
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	-	00.5%	08.4%	00.9%		
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	•	70.00/	92.90/	96.00/	<0.001	<0.001
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						
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 <a href="#"><a href="#"><a href="#">&lt;0.001</a> &lt;0.001</a>  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 <a href="#"><a href="#"><a href="#"><a href="#">&lt;0.001</a> &lt;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%  primary payer  Self-pay 4.9% 2.8% 1.4%  No charge 0.5% 0.4% 0.2%  Other 2.8% 2.6% 1.8%</a></a></a></a>	-		7			
Native American         0.5%         0.0%         0.2%           Other         3.6%         4.3%         2.4%           Household Income          <0.001						
Other         3.6%         4.3%         2.4%           Household Income         <0.001						
Household Income						
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		3.6%	4.3%	2.4%		
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	< 0.001
3rd quartile       24.6%       24.7%       26.0%         4th quartile       22.0%       32.3%       27.4%         Paying modality       <0.001	_	26.6%	20.7%	21.9%		
4th quartile       22.0%       32.3%       27.4%         Paying modality       <0.001		26.8%	22.4%	24.6%		
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%		24.6%	24.7%	26.0%		
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%	4 <sup>th</sup> quartile	22.0%	32.3%	27.4%		
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%	Paying modality				< 0.001	< 0.001
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%	Medicare-primary payer	51.3%	34.6%	68.0%		
primary payer       Self-pay     4.9%     2.8%     1.4%       No charge     0.5%     0.4%     0.2%       Other     2.8%     2.6%     1.8%	Medicaid-primary payer	5.7%	6.2%	3.9%		
Self-pay       4.9%       2.8%       1.4%         No charge       0.5%       0.4%       0.2%         Other       2.8%       2.6%       1.8%	Private insurance-	34.8%	53.5%	24.6%		
No charge         0.5%         0.4%         0.2%           Other         2.8%         2.6%         1.8%	primary payer					
Other 2.8% 2.6% 1.8%	Self-pay	4.9%	2.8%	1.4%		
	No charge	0.5%	0.4%	0.2%		
Admission type, Non- 72.6% 76.9% 77.2% 0.550 <0.001	Other	2.8%	2.6%	1.8%		
	Admission type, Non-	72.6%	76.9%	77.2%	0.550	< 0.001

elective					
Admission day, Weekday	16.0%	16.5%	18.0%	0.045	< 0.001
Single coronary vessel	73.3%	71.9%	71.3%	0.496	< 0.001
revascularization					
Multivessel coronary	17.8%	19.3%	19.9%	0.336	< 0.001
revascularization					
Bifurcation stenting	1.7%	1.3%	1.6%	0.133	0.092
Use of left ventricular	3.3%	6.6%	4.8%	< 0.001	< 0.001
assist device or intra-					
aortic balloon pump					
Cardiogenic shock at	2.8%	4.8%	3.7%	0.001	< 0.001
presentation					
ST-Elevation myocardial	21.3%	22.8%	19.4%	< 0.001	< 0.001
infarction					
Non-ST-elevation	22.9%	26.3%	29.3%	< 0.001	< 0.001
myocardial infarction					
Fractional Flow Reserve	0.7%	0.7%	1.3%	0.004	< 0.001
pressure wire used during					
percutaneous coronary					
intervention					
Intravascular ultrasound	4.8%	7.6%	6.2%	0.005	< 0.001
used during percutaneous	_				
coronary intervention					
Bare-metal stent	28.3%	30.9%	38.6%	< 0.001	< 0.001
implanted					
Drug-eluting stent	73.2%	70.3%	62.9%	< 0.001	< 0.001
implanted					
History of coronary	94.6%	93.4%	92.3%	0.025	< 0.001
artery disease	<i>y</i>				
History of percutaneous	18.7%	20.3%	16.9%	< 0.001	< 0.001
coronary intervention					
History of coronary	7.3%	7.4%	6.8%	0.238	0.017
artery bypass grafting					
History of myocardial	13.2%	13.9%	12.1%	0.005	0.006
infarction					
History of	3.8%	3.5%	4.2%	0.053	0.005
cerebrovascular incident					
Acquired immune	0.1%	1.0%	0.6%	0.012	< 0.001
deficiency syndrome	- · · · · ·	· · •	•		
Alcohol abuse	2.0%	1.9%	1.1%	0.002	< 0.001
Smoker	35.2%	31.4%	27.0%	< 0.001	< 0.001
Rheumatoid	1.8%	1.4%	2.9%	< 0.001	<0.001
	1.070	1.170	<b>2.</b> 770		

arthritis/collagen vascular					
disease					
Congestive heart failure	1.0%	1.7%	2.2%	0.088	< 0.001
Chronic obstructive	15.5%	15.0%	17.6%	< 0.001	< 0.001
pulmonary disease					
Diabetes mellitus,	33.2%	23.4%	29.6%	< 0.001	< 0.001
uncomplicated					
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 <sup>+</sup>	65.9%	59.2%	58.4%	0.358	< 0.001
Obesity <sup>++</sup>	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	10.4%	7.2%	10.5%	< 0.001	< 0.001
disorders					
Paralysis	0.7%	1.0%	0.7%	0.076	0.209
Dementia	1.4%	0.6%	1.2%	0.001	0.001
History of leukaemia	0.3%	1.2%	1.4%	0.238	< 0.001
History of solid tumour	1.2%	1.5%	2.7%	< 0.001	< 0.001
without metastasis					

<sup>\*</sup>Comparison of Hodgkin's vs Non-Hodgkin's lymphoma group; \*\* Comparison of No lymphoma vs. Lymphoma group

<sup>&</sup>lt;sup>+</sup>Increased plasma concentration of cholesterol carried in low-density lipoproteins (LDL) and/or increased total cholesterol in plasma

<sup>&</sup>lt;sup>++</sup>Defined as body mass index ≥30 kg/m<sup>2</sup>

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

Variable	No Lymphoma	Hodgkin's	Non-Hodgkin's	p-	p-
	Diagnosis	Lymphoma	Lymphoma	value*	value**
	(N=7,101,487)	(N=3,516)	(N=14,536)		
Bleeding	3.0%	5.0%	7.7%	< 0.001	< 0.001
complication				Q	<b>Y</b>
Vascular	3.3%	5.8%	7.8%	0.001	< 0.001
complications					
Cardiac	2.4%	2.6%	3.0%	0.098	< 0.001
complications			45		
Post-procedural	3.0%	2.8%	3,6%	0.031	< 0.001
stroke/TIA					
Any	8.1%	10.1%	13.5%	< 0.001	< 0.001
complication			<i>'</i>		
In-hospital	1.6%	2.1%	2.7%	0.096	< 0.001
mortality		\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \			

<sup>\*</sup>Comparison of Hodgkin's vs Non-Hodgkin's Lymphoma group; \*\* Comparison of No lymphoma vs. Lymphoma group

**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	р-	Hodgkin's	p-	Non-	p-
	vs.	value	Lymphoma	value	Hodgkin's	value
	No-		vs. No-		Lymphoma	
	Lymphoma		Lymphoma		vs. No-	
					Lymphoma	
Bleeding	1.12 (1.06-	< 0.001	1.12 (1.05-	< 0.001	0.99 (0.84-	0.461
complication	1.19)		1.20)		1.18)	
Vascular	1.11 (1.05-	< 0.001	1.13 (1.06-	0.001	1.09 (0.92-	0.134
complications	1.18)		1.20)	77	1.28)	
Cardiac	1.07 (0.98-	0.128	1.06 (0.96-	0.190	0.91 (0.72-	0.288
complications	1.17)		1.17)		1.16)	
Post-procedural	1.75 (1.61-	< 0.001	1.82 (1.67-	< 0.001	1.31 (1.05-	0.014
stroke/TIA	1.90)		1.99)		1.63)	
Any	1.31 (1.25-	< 0.001	1.31 (1.25-	< 0.001	1.01 (0.89-	0.601
complication	1.37)		1.38)		1.14)	
In-hospital	1.39 (1.25-	< 0.001	1.40 (1.24-	< 0.001	1.03 (0.77-	0.442
mortality	1.54)		1.56)		1.38)	

<sup>\*</sup>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, multi-vessel 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

**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	Non-Hodgkin's Lymphoma	p-value*
	(N=2718)	(N=2704)	
Bleeding complication	6.0%	4.7%	0.028
Vascular complications	6.8%	4.9%	0.002
Cardiac complications	2.2%	2.7%	0.054
Post-procedural 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

<sup>\*</sup>Propensity score-matched analysis used exact matching on age while additional covariates in the model were sex, Charlson Comorbidity Index, day of admission, non-elective 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.

**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	Lymphoma	p-value*
	(N=3588)	(N=3588)	
Bleeding complication	7.2%	8.4%	< 0.001
Vascular complications	5.1%	7.2%	< 0.001
Cardiac complications	2.8%	3.8%	< 0.001
Post-procedural 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

<sup>\*</sup>Propensity score-matched analysis used exact matching on age while additional covariates in the model were sex, Charlson Comorbidity Index, day of admission, non-elective 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.