Clinical Outcomes in Patients with Pulmonary Hypertension Undergoing Total Hip Arthroplasty

David Kim, MD · Kethy Jules-Elysee, MD · Lauren Turteltaub, MD · Michael K. Urban, MD, PhD · Jacques T. YaDeau, MD, PhD · Shane Reid, BA · Stephen Lyman, PhD · Yan Ma, PhD

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Abstract *Background:* Pulmonary hypertension (PH) is regarded as a risk factor for perioperative complications in patients undergoing noncardiac surgery. *Questions/Purposes:* The objective of this retrospective case-control study was to evaluate the adverse outcomes of pulmonary hypertension patients undergoing elective unilateral hip replacements. *Methods:* We performed a retrospective case-control study of total hip replacement patients with pulmonary hypertension (cases) and without pulmonary hypertension (control). From the years 2003 to 2008, we identified a total of 132 patients undergoing primary total hip replacements with a diagnosis of pulmonary hypertension (right ventricular systolic pressure >35). The primary outcome assessed was the incidence of adverse events that occurred during the postoperative hospital stay. Secondary outcomes studied included length of hospital stay, mortality, and ability to reach certain physical therapy milestones. *Results:* The PH group had significantly more adverse events than the control group. Nonlethal cardiac dysrhythmias comprised the most common adverse outcome among the PH group. Overall, the PH group had a morbidity rate of 34.7% while the control had a rate of 21%. The PH group had longer hospital stay

(6.7 days vs. 5.9). Both groups had zero mortality during the hospital stay. The PH group had comparable rehabilitation recovery times than the control group. *Conclusion:* This retrospective case-control study demonstrates that pulmonary hypertension patients undergoing total hip arthroplasty are more prone to adverse outcomes, especially cardiac dysrhythmias, and longer hospital stays.

Keywords pulmonary hypertension · perioperative complications · outcomes · total hip arthroplasty

Introduction

Pulmonary hypertension (PH), either primary or secondary, is regarded as a risk factor for adverse outcomes in patients undergoing joint replacement, especially when the possibility of an embolic event, either from the intraoperative emboli of bone marrow, cement, and bone during reaming or from postoperative deep vein thrombosis and subsequent pulmonary emboli (PE), is higher in this surgical population [8]. PE can worsen the pulmonary hypertension, leading to acute right ventricular failure, persistent postoperative hypoxemia, and coronary ischemia [1].

Patients with PH are often advised against elective noncardiac surgery based on the higher morbidity and mortality cited by previous case reports and retrospective studies [2]. Ramakrishna et al. published a study assessing outcomes of pulmonary hypertension patients undergoing noncardiac surgery in 2005 [8]. This study reported an incidence of early mortality (≤ 30 days) at 7% and an incidence of morbidity at 42%. Another study in 2010 by Memtsoudis et al. revealed that pulmonary hypertension patients undergoing major joint replacements (both total hip and knee arthroplasties) are at increased risk for perioperative mortality, 4- and 4.5-fold increased risk, respectively [6]. However, there remains to be only a few studies analyzing the risk of adverse events and mortality in

Level of Evidence: Level III: Prognostic Study.

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D. Kim, MD (✉) · K. Jules-Elysee, MD · L. Turteltaub, MD · M. K. Urban, MD, PhD · J. T. YaDeau, MD, PhD · S. Reid, BA · S. Lyman, PhD
Department of Anesthesiology, Hospital for Special Surgery,
535 East 70th Street,
New York, NY 10021, USA
e-mail: kimd@hss.edu

S. Lyman, PhD · Y. Ma, PhD
Division of Biostatistics and Epidemiology,
Department of Public Health, Weill Cornell Medical College,
New York, NY 10065, USA

pulmonary hypertension patients undergoing joint replacements.

Pulmonary hypertension is not an absolute contraindication to joint replacement. The objective of this retrospective case–control study was to see whether these patients can undergo a hip replacement safely, with minimal adverse events and mortality, achieving similar length of hospital stay and reaching physical therapy milestones as their matched non-pulmonary hypertension counterparts. We hypothesized that patients with pulmonary hypertension will not have more adverse events and longer hospital stays and will be able to reach the physical therapy milestones in a timely manner.

Questions remain whether PH patients can safely undergo joint replacements that are known to cause pulmonary embolic events intraoperatively and postoperatively. The primary aim of this study was to address which are the most common adverse events associated with pulmonary hypertension in patients undergoing hip replacements. Additionally, secondary questions included whether PH patients stay longer in the hospital and if they are at a higher risk for mortality. Finally, we wished to determine if they can also reach typical rehabilitation milestones during the initial postoperative hospital stay.

Patients and Methods

The study was approved by the Hospital for Special Surgery Institutional Review Board. We performed a retrospective case–control study of total hip replacement patients with pulmonary hypertension (cases) and without pulmonary hypertension (control). Medical records were reviewed from the years 2003 to 2008. We identified a total of 132 patients undergoing primary total hip replacements with an International Classification of Disease, ninth revision, Clinical Modification (ICD-9-CM) diagnosis of pulmonary hypertension upon discharge (2-D echo with a right ventricular systolic pressure >35). We then matched both PH and non-PH groups based on surgeon, date of surgery (± 30 days), patient age (± 5 years), and body mass index (BMI) (± 5). After excluding 17 patients, to whom we either could not match (13) or the severity of PH was not identified (4), we ended up with 115 patients with various degrees of pulmonary hypertension based on pulmonary artery systolic pressures (PASP) (mild=82 (PASP 35–45), moderate=26 (PASP 45–59), severe=7 (PASP>60)) and matched them to 115 patients with no pulmonary hypertension.

After successfully matching the case group to the control, the final study population had the following preoperative characteristics (see Tables 1 and 2): mean ages of 73.3 and 73.0, mean BMI of 26.2 and 26.3, and mean American Society of Anesthesiologists (ASA) Class of 2.6 and 2.3 for the pulmonary hypertension group and control, respectively. The pulmonary hypertension group had higher incidences of preoperative comorbidities than the control group: previous myocardial infarction (10 vs. 4, p value=0.049), chronic obstructive pulmonary disease (COPD) (16 vs. 8, p value=0.042), abnormal stress test (12 vs. 5, p value=0.039), and atrial fibrillation (27 vs 6, p value=0.0001). The majority of

Table 1 Patient characteristics

Characteristic	PH	Control
Age, mean (SD)	73.3 (10)	73.0 (9.9)
BMI, mean (SD)	26.2 (5)	26.3 (4.7)
ASA classification (I–III), mean (SD)	2.6 (.5)	2.3 (.5)
Female, N (%)	79 (68.7%)	69 (60%)
Male, N (%)	36 (31.3%)	46 (40%)

PH pulmonary hypertension, BMI body mass index, ASA American Society of Anesthesiologists, SD standard deviation

the case group had mild (71%) or moderate (23%) degrees of pulmonary hypertension with only 6% presenting with severe pulmonary hypertension.

Intraoperative characteristics between the pulmonary hypertension group and the control group were similar (Table 3). The majority of the surgeries were done under a neuraxial technique (99% in both groups). The length of surgery was similar in both groups (1.5 vs 1.3 h). The number of cement bags used was similar (1.71 vs 1.68). Both intraoperative blood pressures were similar ranging from a systolic blood pressure (SBP) of 82 to 142 (case) vs 84 to 147 (control), and postoperative blood pressure were similar (SBP 120 vs 119). A little more than half of the patients from both groups underwent controlled hypotension (65 vs 63), and epinephrine was used in two thirds of the patients (76 vs 79).

Upon reviewing progress notes, intraoperative anesthesia records, postoperative care unit records, and surgical notes, we collected the following: (1) comorbidities; (2) type and duration of surgery; (3) type of intraoperative monitoring and anesthesia; (4) use of cement during surgery; (5) intraoperative course; (6) length of postanesthesia care unit (PACU)/hospital stay; (7) postoperative course including radiographic, hemodynamic, and laboratory abnormalities such as arterial blood gases; and (8) adverse outcomes including respiratory complications, cardiac arrhythmias (e.g., atrial fibrillation with rapid ventricular rate), congestive heart failure (CHF), myocardial ischemia (MI), PE, fat embolism syndrome (FES), altered mental status (AMS), and death.

Statistical Analysis

Descriptive statistics will include mean/median and standard deviations for continuous variables and frequencies/percentages for discrete variables. Inferential analysis will incorporate t tests or the appropriate nonparametric equivalent tests for analysis of time-to-milestone, length of PACU stay, and length of hospital stay. A logistic regression model was constructed to identify the risk factors for the length of hospital stay. Specifically, a binary outcome based on the length of hospital stay was created using 5 days as the cutoff point. Patients' characteristics (age, gender, BMI, American Society of Anesthesiologists (ASA) Classification), the severity of pulmonary hypertension, previous MI, abnormal stress test, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), length of PACU stay, time to

Table 2 Incidence of comorbidities between pulmonary hypertension group and control group

	MI	HTN	Abn stress test	COPD	Asthma	Smoker	DM	Afib
PH	10 (9%)	65 (56%)	12 (10%)	16 (14%)	10 (9%)	10 (9%)	10 (9%)	27 (23%)
Control	4 (3%)	61 (53%)	5 (4%)	8 (7%)	7 (6%)	10 (9%)	5 (4%)	6 (5%)
<i>p</i> value*	0.049	0.298	0.039	0.042	0.225	0.5	0.091	0.0001

MI myocardial infarction, HTN hypertension, Abn Stress Test abnormal stress test, COPD chronic obstructive pulmonary disorder, DM diabetes mellitus, Afib atrial fibrillation, PH pulmonary hypertension

* $p < 0.05$ was considered significant

physical therapy milestone (out of bed, ambulate with assistance, climb stairs), and complications (respiratory complications, cardiac dysrhythmia, CHF, ischemia/MI, AMS, FES, PE) were included as predictors in the logistic regression model. Stepwise elimination was used to select predictors, and only statistically significant predictors were retained in the model. Odds ratio (OR), 95% confidence interval of OR, and *p* value were reported. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC) and SPSS 19 for Windows.

Results

The PH group experienced significantly more adverse events than the control group ($p = 0.0093$; Table 4). Interestingly, respiratory complications were not the most frequent adverse outcome as it was in the other studies [8]. Nonlethal cardiac dysrhythmias, including supraventricular tachycardia, atrial fibrillation with rapid ventricular rate, bradycardia, and sinus tachycardia, comprised the most common adverse events among the PH group. Overall, the

PH group had an adverse event rate of 34.7% while the control had a rate of 21%. There were no deaths reported in either groups during the hospital stay.

The pulmonary hypertension group had longer hospital stays (6.7 vs. 5.9 days, $p = 0.0021$, Table 5) and length of PACU stay (16 vs. 13.5 h) compared to the control group. There was a higher frequency of admitting the PH group into the Step Down Unit (19 vs 7) and transferring to New York Hospital (NYH), a level one facility equipped with intensive care units (4 vs 1).

A logistic regression analysis performed to identify the predictors of length of hospital stay (Table 6) in patients with pulmonary hypertension indicated that moderate PH, obesity, COPD, length of PACU stay, ambulation with assistance, and abnormal stress test increased the likelihood of a PH patient to stay longer than 5 days.

The pulmonary hypertension group had comparable rehabilitation recovery times than the control group (see Table 5) including the ability to get out of bed (1.2 vs 1.2 days, p value=0.4442), ambulate with assistance (1.4 vs 1.3 days, p value=0.1065), and climb stairs (3.9 vs 3.6 days, p value=0.2062).

Table 3 Intraoperative characteristics

	Control (n)	Control (%)	PH (n)	PH (%)
Type of anesthesia				
CSE	88	77	80	70
Epidural	4	3.5	11	9.7
Epidural+LPB	14	12	15	13
General+LPB	1	0.8	0	0
CSE+LPB	6	5	3	2.6
Spinal	2	1.8	4	3.5
General	0	0	1	0.8
Invasive monitoring				
CVP catheter	39	42	57	50
PAC catheter	0	0	8	7
Controlled hypotension				
Yes	65	57	63	55
No	49	43	52	45
Epinephrine				
Yes	76	66	79	69
No	39	34	36	31
Hours of surgery				
Mean	1.269		1.544	
SD	0.501		0.704	
No. of cement bags				
Mean	1.688		1.708	
SD	1.23		1.05	

CSE combined spinal–epidural, LPB lumbar plexus block; CVP central venous pressure; PAC pulmonary artery catheter; SD standard deviation

Discussion

While pulmonary hypertension is not a contraindication for joint replacement, it is regarded as a risk factor for patients undergoing hip arthroplasty due to its possible derangement

Table 4 Perioperative complications

Morbidity	PH patients (n)	Frequency (%)	Control (n)	Frequency (%)	<i>p</i> value $\diamond$
Respiratory complications	4	4/115=3.5	3	3/115=2.6	0.5
Cardiac dysrhythmia ^a	24	24/115=20.9	6	6/115=5	0.0002
CHF	1	1/115=0.9	2	2/115=1.7	0.5
Ischemia/MI	2	2/115=1.7	0	0/115=0	0.251
AMS	5	5/115=4.3	5	5/115=4.3	0.5
FES	2	2/115=1.7	6	6/115=5.2	0.1402
PE	2	2/115=1.7	2	2/115=1.7	0.6891
Total	40	40/115=34.7	24/115	24/115=21	0.0093

^aNo dysrhythmias required defibrillation

CHF congestive heart failure, MI myocardial infarction, AMS acute mental status; FES fat embolism syndrome; PE pulmonary embolism $\diamond p < 0.05$ were considered significant

Table 5 Physical therapy milestones and length of hospital stay

	Control (SD)	PH (SD)	<i>p</i> value*
POD out of bed	1.2 (0.48)	1.191 (0.46)	0.4442
POD amb with assist	1.296 (0.546)	1.4 (0.711)	0.1065
POD climbing stairs	3.622 (1.874)	3.929 (1.568)	0.2062
Length of hospital stay (days)	5.87 (1.885)	6.704 (2.449)	0.0021

POD postoperative day, SD standard deviation, amb ambulation

* $p < 0.05$ was considered significant

of pulmonary and cardiovascular functions [2, 4, 6–8]. Awareness of potential complications from this surgical population may guide clinical decisions and alter patient management practices to optimize perioperative outcomes [8]. The overall aims of this retrospective study were to examine total hip replacement patients, both with and without pulmonary hypertension, and evaluate the incidence of adverse events and mortality, measure length of hospital stay, and compare rehabilitation achievements.

This study has demonstrated that PH patients are more likely to have adverse perioperative outcomes and longer hospital stays.

There are several limitations to this case-control study. The matching process for the control group may have excluded important covariates. By limiting the selection process to age, body mass index, date of surgery, and surgeon, it is possible that the control group did not take into account other key risk factors known to be associated with higher adverse outcomes, longer hospital stays, and mortality, such as ASA class. However, as demonstrated in Table 2 (demographics), the pulmonary hypertension group was significantly associated with more comorbidities (chronic obstructive pulmonary disease, atrial fibrillation, and coronary artery disease). Finding matches for relatively unhealthy patients in the given time frame, with the same surgeon would have likely caused several exclusions, limiting the number of patients for analysis. Another limitation of the study is that the PH patients were not followed post-discharge. The mortality rate in our study was zero. However, we did not follow our patients 30 days out as

other studies have done. This study also has the limitations of being a retrospective study with possible selection bias. Another limitation is that since the patients came from a single institution that incorporates a specific methodology and protocol in intra- and postoperative care (e.g., regional anesthesia and epidural PCA for intraoperative anesthetic and postoperative pain management), there is an institutional bias on how these patients are cared for in the perioperative period.

The literature on PH patients undergoing elective noncardiac surgery is scarce. One large retrospective study done in 2005 by Ramakrishna et al. included 145 PH patients undergoing noncardiac surgery and cited a morbidity rate of 48% for orthopedic surgeries and a mortality rate of 7% [8]. The most common perioperative morbidity were respiratory failure (28% of patients, including pneumonia, hypoxia requiring oxygen, or prolonged intubation), cardiac dysrhythmias (12% of patients, including new-onset atrial fibrillation, supraventricular tachycardia, bradycardia, or ventricular tachycardia/fibrillation), and congestive heart failure (11% of patients) [5]. Another study by Kaw et al. included 96 PH patients undergoing noncardiac surgery and had a morbidity of 28% and mortality of 1% [2]. This study's most common morbidity was perioperative congestive heart failure (13%). Similarly, a recent study by Lai et al. showed a major adverse event rate of 24% and a mortality of 9.7% in 62 patients with severe PH undergoing noncardiac surgery [4]. This study's most common adverse events were delayed tracheal extubation (21%) and heart failure (9.7%).

Our study showed a morbidity rate of 34.7% and a mortality rate of zero. The most common adverse event was not respiratory failure (only 3.5% of PH patients) but cardiac dysrhythmias (20.9% of PH patients). The much higher incidence in cardiac dysrhythmias in our PH patients could be a reflection of this particular group's low threshold and susceptibility to arrhythmias in the setting of a likely embolic event during joint replacements. One plausible explanation is that a small embolic event in the PH patient may have worsened their pulmonary hypertension, leading to cardiac ischemia and arrhythmias [8]. Notably, as seen in Table 2 (demographics), PH patients had much higher rates of atrial fibrillation (23%). The findings of higher incidences of cardiac dysrhythmias preoperatively affirm other studies [2, 7] that have showed the incidence of new-onset atrial fibrillation and flutter is as high as 25.1% in patients with PH. We agree that the patients with baseline arrhythmias are more susceptible to have unstable arrhythmias postoperatively, but it may be that PH patients at baseline are more susceptible to having arrhythmias and the worsening of those arrhythmias during the perioperative period could be attributed to an intra- or postoperatively ischemic or embolic event.

Unlike the Ramakrishna study, which was done under general anesthesia, almost all of our PH patients underwent regional anesthesia (99% of patients either had an epidural or CSE), which may explain the considerable difference in respiratory complications. In our study, there was no significant difference in respiratory complications between the PH patients and the control group. Since regional anesthesia

Table 6 Logistic regression analysis

Morbidity	Odds ratio	95% confidence interval	<i>p</i> value*
Pulm HTN—mild	1.312	(0.687, 2.503)	0.4106
Pulm HTN—moderate	3.32	(1.04, 10.598)	0.0427
Pulm HTN—severe	1.454	(0.222, 9.538)	0.6962
Obesity (BMI 30–39.9)	2.333	(1.06, 5.136)	0.0354
Overweight (BMI 25–29.9)	1.756	(0.879, 3.509)	0.111
COPD	0.282	(0.091, 0.873)	0.0282
Length of PACU stay	1.029	(1.001, 1.056)	0.039
POD ambulation with assistance	1.905	(1.066, 3.404)	0.0295

Pulm HTN pulmonary hypertension, BMI body mass index, COPD chronic obstructive pulmonary disease, PACU postanesthesia care unit, POD postoperative day

* $p < 0.05$ was considered significant

provides optimal pain management [10] and minimizes opioid use, the likelihood of oversedation, respiratory depression, and hypoxemia is small [9]. By optimizing perioperative pain control with a patient-controlled epidural analgesia (PCEA), reductions in postoperative inflammation and sympathetic nerve activity [3] will moderate a patient's pain level and potentially minimize the severity of pulmonary hypertension [4]. However, regional anesthesia is our institution's preferred method of anesthesia (only 1 out of 230 patients in the study had general anesthesia). There are cases that optimal control of ventilation is important to prevent hypoxemia and hypercarbia and the possibility of worsening pulmonary hypertension.

Although PH achieved physical therapy milestones in a time course similar to the control, there was a statistically significant difference in the length of stay (LOS). We assessed physical therapy milestones as an objective measure of the patient's functional status in the postoperative period. A severely debilitated patient would not be able to ambulate in a timely manner. Using a logistic regression analysis, we found that obesity, chronic obstructive pulmonary disease, abnormal stress test, moderate pulmonary hypertension, length of PACU stay, and ambulation with assistance were predictors of increasing LOS. Interestingly, severe pulmonary hypertension patients were not found to be predictors. This is most likely due to the paucity of ($n=7$) severe PH patients enrolled in the study to reach statistical significance.

The regression analysis reaffirms certain comorbidities (coronary artery disease, chronic obstructive pulmonary disease) are associated with longer hospital stays. It also reaffirms that the longer PACU (ICU) stay and the delayed ability to ambulate were shown to be a predictor of length of stay. But most importantly, it verifies that moderate pulmonary hypertension is a predictor of longer hospital stays. However, given that the pulmonary hypertension group had more comorbidities, the increased LOS may be a reflection of their higher ASA class rather than their pulmonary hypertension status. Future studies are needed to analyze the predictors of morbidity among PH patients.

In conclusion, our retrospective case-control study demonstrated that pulmonary hypertension patients undergoing total hip arthroplasty are more prone to adverse events and longer hospital stays.

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Disclosures

Conflict of Interest: David Kim, MD, Kethy Jules-Elysee, MD, Shane Reid, BA, Michael K. Urban, MD, PhD, Lauren Turteltaub, MD, Jacques T. YaDeau, MD, PhD, and Stephen Lyman, PhD have declared that they have no conflict of interest. Yan Ma, PhD reports grants from NIH and AHRQ during the conduct of the study.

Human/Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed Consent: Informed consent was obtained from all patients for being included in the study.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

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