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Association Between Use of Enhanced Recovery After Surgery Protocol and Postoperative Complications in Total Hip and Knee Arthroplasty in the Postoperative Outcomes Within Enhanced Recovery After Surgery Protocol in Elective Total Hip and Knee Arthroplasty Study (POWER2)

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Supplemental content

IMPORTANCE The Enhanced Recovery After Surgery (ERAS) care protocol has been shown to improve outcomes compared with traditional care in certain types of surgery.

OBJECTIVE To assess the association of use of the ERAS protocols with complications in patients undergoing elective total hip arthroplasty (THA) and total knee arthroplasty (TKA).

DESIGN, SETTING, AND PARTICIPANTS This multicenter, prospective cohort study included patients recruited from 131 centers in Spain from October 22 through December 22, 2018. All consecutive adults scheduled for elective THA or TKA were eligible for inclusion. Patients were stratified between those treated in a self-designated ERAS center (ERAS group) and those treated in a non-ERAS center (non-ERAS group). Data were analyzed from June 15 through September 15, 2019.

EXPOSURES Total hip or knee arthroplasty and perioperative management. Sixteen individual ERAS items were assessed in all included patients, whether they were treated at a center that was part of an established ERAS protocol or not.

MAIN OUTCOMES AND MEASURES The primary outcome was postoperative complications within 30 days after surgery. Secondary outcomes included length of stay and mortality.

RESULTS During the 2-month recruitment period, 6146 patients were included (3580 women [58.2%]; median age, 71 [interquartile range (IQR), 63-76] years). Of these, 680 patients (11.1%) presented with postoperative complications. No differences were found in the number of patients with overall postoperative complications between ERAS and non-ERAS groups (163 [10.2%] vs 517 [11.4%]; odds ratio [OR], 0.89; 95% CI, 0.74-1.07; *P* = .22). Fewer patients in the ERAS group had moderate to severe complications (73 [4.6%] vs 279 [6.1%]; OR, 0.74; 95% CI, 0.56-0.96; *P* = .02). The median overall adherence rate with the ERAS protocol was 50.0% (IQR, 43.8%-62.5%), with the rate for ERAS facilities being 68.8% (IQR, 56.2%-81.2%) vs 50.0% (IQR, 37.5%-56.2%) at non-ERAS centers (*P* < .001). Among the patients with the highest and lowest quartiles of adherence to ERAS components, the patients with the highest adherence had fewer overall postoperative complications (144 [10.6%] vs 270 [13.0%]; OR, 0.80; 95% CI, 0.64-0.99; *P* < .001) and moderate to severe postoperative complications (59 [4.4%] vs 143 [6.9%]; OR, 0.62; 95% CI, 0.45-0.84; *P* < .001) and shorter median length of hospital stay (4 [IQR, 3-5] vs 5 [IQR, 4-6] days; OR, 0.97; 95% CI, 0.96-0.99; *P* < .001).

CONCLUSIONS AND RELEVANCE An increase in adherence to the ERAS program was associated with a decrease in postoperative complications, although only a few ERAS items were individually associated with improved outcomes.

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An estimated 310 million patients undergo surgery worldwide each year.[1] In the United States, 1 million total hip arthroplasty (THA) and total knee arthroplasty (TKA) procedures are performed annually, with an expectation of growth in the coming years.[2] The International Surgical Outcomes Study[3] showed that 16.5% of patients who underwent orthopedic surgery experienced complications. The incidence of complications in THA and TKA was 3.2% to 8.0%,[4] with an important variability between centers.[4,5] Postoperative complications after THA and TKA have been shown to increase hospital length of stay (LOS).[6] Kehlet[7] described the concept of the multimodal approach to recovery in 1997. The Enhanced Recovery After Surgery (ERAS) program that entails an evidenced-based protocol based on a wide literature search was initiated by Ljungqvist et al[8] in the ERAS study group, which later developed into the ERAS Society. The ERAS protocol includes a variable number of multidisciplinary perioperative measures whose initial goal is to improve recovery and reduce morbidity, which will result in secondary benefits, including reductions in LOS, convalescence, and costs.[9] Observational studies[10] and randomized clinical trials[11] have shown that ERAS was associated with improved outcomes in patients undergoing THA and TKA, mainly a decrease in LOS.[12,13]

Until the recent publication of the ERAS Society THA and TKA guidelines,[14] the most accepted recommendations were those proposed by Soffin and YaDeau in 2016.[15] ERAS in THA and TKA share the same problems as ERAS in other surgical procedures: adoption is slow,[16] and adherence to ERAS guidelines is low.[17]

The aim of this study was to characterize the management strategies for patients who underwent elective THA or TKA, including centers with and without an established ERAS protocol. The primary end point was the incidence of postoperative complications. Secondary end points were LOS and the potential associations between the adherence to the individual ERAS items and the occurrence of postoperative complications.

Key Points

Question How frequent are complications after total hip and knee arthroplasty procedures and how are the Enhanced Recovery After Surgery (ERAS) protocols associated with them?

Findings In this large, multicenter cohort study that included 6146 patients in 131 hospitals, 680 (11.1%) presented with postoperative complications and 352 (5.7%) presented with complications graded as moderate to severe. Patients who had greater compliance with the ERAS items had fewer postoperative complications, regardless of whether or not the center had an established ERAS protocol.

Meaning Although only a few perioperative interventions were associated with decreased complications, greater adherence with the set of ERAS measures was associated with a decrease in postoperative complications at 30 days of follow-up.

Methods

Study Design and Participants

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline[18] and the Reporting on ERAS Compliance, Outcomes, and Elements Research (RECOVER) Checklist.[19] Hospital and investigator engagement was facilitated through the Spanish Perioperative Audit and Research Network (REDGERM), which was established by the Grupo Español de Rehabilitación Multimodal (GERM). All hospitals in Spain were invited to participate regardless of the number of beds and the existence of an ERAS protocol.

The Postoperative Outcomes Within Enhanced Recovery After Surgery Protocol in Elective Total Hip and Knee Arthroplasty (POWER2) study was a prospective 2-month multicenter cohort study. The study was approved by the Instituto Aragonés de Ciencias de la Salud Ethics Committee, Zaragoza, Spain, and the Spanish Medical Agency and was registered prospectively in an international trial registry.[20] The study protocol, technical appendix, and other documents are available at http://www.grupogerm.es/power2, and the study protocol has been published.[21]

The ethics committees or institutional review boards at each site reviewed and approved the protocol. Written informed consent was obtained from all participants.

Procedures

All consecutive adult patients (aged >18 years) undergoing elective primary THA or TKA were included during a single period of recruitment from October 22 through December 22, 2018, in each participating center. Each patient was followed up for 30 days after surgery. The follow-up was performed through hospital and primary care medical records.

Data were collected using Castor Electronic Data Capture[22] and anonymized before entry onto a secure Internet-based electronic case record form designed specifically for POWER2. Participating hospitals were considered self-proclaimed ERAS centers in cases in which a multidisciplinary clinical pathway was implemented, regardless of the perioperative items that conformed to the pathway and whether hospitals were audited regularly. Individual data on 16 ERAS items were collected prospectively for each included patient. The definition of the individual ERAS components was based on the recommendations of Soffin and YaDeau[15] (eTable 1 in the Supplement). Data included patient characteristics (American Society of Anesthesiologists [ASA] score, age, sex, smoking status, body mass index, clinical frailty score, and comorbidities), procedure performed, surgical approach, perioperative interventions, adherence to ERAS items, and outcomes (including postoperative complications, time to achieve targeted mobility, LOS, and 30-day mortality). Complications were defined and graded as mild, moderate, or severe according to international recommendations[21,23-26] (eTable 2 in the Supplement) and were included if they occurred within 30 days after surgery. Data validation was conducted by specific validators at each site. A minimum sample size of 3012 was estimated, expecting 50% of patients with at least 1 complication, a 95% confidence level, and 3% accuracy.

Outcomes

The primary outcome was the number of patients with 30-day in-hospital postoperative complications. Secondary outcome measures included the number of patients with 30-day in-hospital postoperative moderate to severe complications, mortality, readmission, reintervention rates, and hospital LOS.

Statistical Analysis

Data were analyzed from March 15 through September 15, 2019. We analyzed outcomes depending on whether the patient received treatment at a hospital that belonged to a self-designated ERAS program (ERAS group). The discrete and continuous variables were described as number (percentage) and median (interquartile range [IQR]), respectively. We analyzed differences using the Fisher exact test for discrete variables and the Pearson and Wilcoxon rank sum tests for continuous variables. Subsequently, we repeated the analysis, subdividing the sample into quartiles according to the real adherence rate to ERAS items (regardless of whether the patient was treated at an ERAS hospital or not) and comparing the quartiles of higher and lower adherence to ERAS items. Next, we analyzed complication rates for each of the ERAS items using the Fisher exact test, and we performed a multivariable logistic regression analysis to study the association of the rate of each of the items with the clinical and demographic variables. We also used the same model in a multilevel multivariable logistic regression model to explore independent factors associated with postoperative complications assessing the variability of each site. Stratification by type of surgery (THA or TKA) was performed for the most relevant outcomes.

We performed several post hoc analyses. To assess the association of the underlying pathologic finding in the included patients, we divided the patients between those with ASA scores of I through II and III through IV (higher scores indicate severe preoperative systemic disease) and analyzed the adherence to ERAS items in these groups, as well as the postoperative outcomes. We performed this analysis for the self-described ERAS centers vs non-ERAS centers and for the ERAS adherence quartiles, depending on the median compliance in each group. Bubble plots were used to graphically illustrate the associations between the percentage of patients with postoperative complications and LOS with the volume of patients recruited at each site. To study the association between the percentage of patients with postoperative complications and LOS and the volume of patients recruited by each center, we used 2 β regression models. Through a linear regression model, we performed a post hoc analysis to evaluate the influence of ERAS items and other perioperative variables in LOS. For this purpose, we performed a univariable and a multivariable analysis. We denoted as statistically significant those comparisons where 2-sided $P < .05$.

Results

Participants

Data describing 6146 patients were collected in 131 hospitals in Spain (**Figure 1**). Of these, 2566 (41.8%) were men and 3580 were women (58.2%); median age was 71 (IQR, 63-76) years. Other characteristics are shown in **Table 1**. No centers or patients were excluded owing to low recruitment. According to the hospitals where the surgeries were performed, 1592 patients (25.9%) were included in self-designated ERAS centers. The ERAS and non-ERAS groups showed demographic differences in the number of patients with hypertension (2747 [60.3%] vs 900 [56.5%]), coronary artery disease (290 [6.4%] vs 70 [4.4%]), atrial fibrillation (336 [7.4%] vs 85 [5.3%]), chronic kidney disease (224 [4.9%] vs 108 [6.8%]), ASA score (ASA III-IV (345 [21.7%] vs 1273 [28.0%]), and duration of surgery (median, 90 [IQR, 75-115] vs 83 [IQR, 65-104] minutes). More patients in the ERAS group received local anesthesia (188 [11.8%] vs 64 [1.4%]) and tranexamic acid (1348 [85.9%] vs 3191 [70.2%]), whereas fewer patients in the ERAS group received epidural (38 [2.4%] vs 350 [7.7%]) or regional (157 [9.9%] vs 770 [16.9%]) anesthesia. Patients in the ERAS group also received fewer crystalloids (median, 800 [IQR, 550-1000] vs 1000 [IQR, 700-1200] mL) and colloids (median, 0 [IQR, 0-250] vs 0 [IQR, 0-0] mL) during surgery as well as fewer red blood cell transfusions (RBCTs) (mean [SD], 9 [0.6%] vs 52 [1.1%]) (Table 1). ERAS adherence quartiles were calculated for all patients from the median overall adherence to the 16 ERAS items, regardless of whether the patient was treated within an ERAS protocol. Adherence in quartile 1 was 43.75% or less; in quartile 2, greater than 43.75% to 50.00%; in quartile 3, greater than 50.00% to 62.50%; and in quartile 4, greater than 62.50%. The quartile with the lowest adherence to ERAS included the most patients (eTable 3 in the Supplement). Patients with lower adherence to ERAS had a higher prevalence of chronic kidney disease (48 [4.4%] vs 103 [5.0%]), had longer duration of surgery (median, 90 [IQR, 74-110] vs 90 [IQR, 75-115] minutes), received more crystalloid during surgery (median, 1000 [IQR, 700-1200] vs 1000 [750-1200] mL), and had more epidural anesthesia (73 [6.8%] vs 149 [7.2%]) and regional analgesia (185 [17.1%] vs 244 [11.8%]) performed compared with the group with greater adherence to ERAS (eTable 3 in the Supplement).

Figure 1. STROBE Flow Diagram for Included Patients

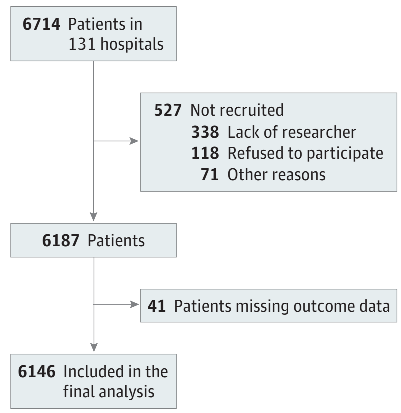


Table 1. Demographic and ERAS Adherence Data[a]

Characteristic	Patient Group All (n = 6146)	No ERAS (n = 4554)	ERAS (n = 1592)
Age, median (IQR), y	71 (63-76)	71 (64-76)	70 (63-76)
Men	2566 (41.8)	1904 (41.8)	662 (41.6)
BMI, median (IQR)	29.3 (26.4-32.9)	29.4 (26.4-32.8)	29.3 (26.4-32.9)
ASA classification[b]			
ASA I	391 (6.4)	262 (5.8)	129 (8.1)
ASA II	4136 (67.3)	3019 (66.3)	1117 (70.2)
ASA III	1575 (25.6)	1238 (27.2)	337 (21.2)
ASA I-II	4257 (73.7)	3281 (72.0)	1246 (78.3)
ASA III-IV	1618 (26.3)	1273 (28.0)	345 (21.7)
Former smoker	1005 (16.4)	758 (16.6)	247 (15.5)
Current smoker	699 (11.4)	505 (11.1)	194 (12.2)
Frailty score, median (IQR)[c]	3 (2-3)	3 (2-3)	3 (2-4)
Hypertension	3647 (59.3)	2747 (60.3)	900 (56.5)
Diabetes	1140 (18.5)	848 (18.6)	292 (18.3)
Coronary arterial disease	360 (5.9)	290 (6.4)	70 (4.4)
Heart failure	158 (2.6)	113 (2.5)	45 (2.8)
Cirrhosis	52 (0.8)	42 (0.9)	10 (0.6)
Stroke	288 (4.7)	226 (5.0)	62 (3.9)
Atrial fibrillation	421 (6.8)	336 (7.4)	85 (5.3)
COPD/asthma	694 (11.3)	522 (11.5)	172 (10.8)
Chronic kidney disease	332 (5.4)	224 (4.9)	108 (6.8)
Peripheral vasculopathy	281 (4.6)	217 (4.8)	64 (4.0)
Rheumatoid arthritis	126 (2.1)	94 (2.1)	32 (2.0)
Dementia	66 (1.1)	55 (1.2)	11 (0.7)
Hemoglobin level, median (IQR), g/dL	14.0 (13.1-15.0)	14.1 (13.1-15.0)	14.0 (13.1-15.0)
Creatinine level, median (IQR), mg/dL	0.80 (0.70-0.95)	0.80 (0.69-0.95)	0.80 (0.70-0.96)
THA	2301 (37.4)	1711 (37.6)	590 (37.1)
TKA	3845 (62.6)	2843 (62.4)	1002 (62.9)
Duration of surgery, median (IQR), min	90 (75-110)	90 (75-115)	83 (65-104)
Anesthesia			
General	460 (7.5)	351 (7.7)	109 (6.8)
Intradural	5679 (92.4)	4202 (92.3)	1477 (92.8)
Epidural	388 (6.3)	350 (7.7)	38 (2.4)
Regional	927 (15.1)	770 (16.9)	157 (9.9)
Local	252 (4.1)	64 (1.4)	188 (11.8)
Crystalloid administered, median (IQR), mL	1000 (700-1200)	1000 (700-1200)	800 (550-1000)
Colloid administered, median (IQR), mL	0 (0-0)	0 (0-0)	0 (0-250)
Red blood cell transfusion	61 (1.0)	52 (1.1)	9 (0.6)
Red blood cell transfused, median (IQR), mL	445 (260-560)	400 (258-500)	715 (525-800)
Blood loss, median (IQR), mL	200 (100-350)	200 (100-350)	200 (100-400)
Tranexamic acid administered	4539 (73.9)	3191 (70.2)	1348 (85.9)
Presurgical education	1688 (27.5)	433 (9.5)	1255 (78.8)
Presurgical optimization	1193 (19.4)	547 (12.0)	646 (40.6)
Preoperative fasting	2997 (48.8)	1831 (40.2)	1166 (73.2)
Patient blood management	2396 (39.0)	1273 (28.0)	1123 (70.5)
Preoperative carbohydrate drinks preload	117 (1.9)	78 (1.7)	39 (2.4)
Avoidance of long-acting sedative premedication	3311 (53.9)	2448 (53.8)	863 (54.2)
Thromboprophylaxis	5655 (92.0)	4120 (90.5)	1535 (96.4)
Antibiotic prophylaxis	6076 (98.9)	4497 (98.7)	1579 (99.2)
Regional anesthesia	4919 (80.0)	3575 (78.5)	1344 (84.4)

(continued)

Table 1. Demographic and ERAS Adherence Data[a] (continued)

Characteristic	Patient Group All (n = 6146)	No ERAS (n = 4554)	ERAS (n = 1592)
PONV prophylaxis	3842 (62.5)	2739 (60.1)	1103 (69.3)
Active prevention of unintentional hypothermia	5082 (82.7)	3734 (82.0)	1348 (84.7)
Goal-directed fluid therapy	591 (9.6)	269 (5.9)	322 (20.2)
Postoperative analgesia	5978 (97.3)	4410 (96.8)	1568 (98.5)
Postoperative glycemic control	3208 (52.2)	2258 (49.6)	950 (59.7)
Early mobilization	2166 (35.2)	984 (21.6)	1182 (74.2)
Early feeding	3953 (64.3)	2563 (56.3)	1390 (87.3)

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COPD, chronic obstructive pulmonary disease; ERAS, Enhanced Recovery After Surgery; IQR, interquartile range; PONV, postoperative nausea and vomiting; THA, total hip arthroplasty; TKA, total knee arthroplasty.

SI conversion factors: To convert albumin to grams per liter, multiply by 10; creatinine to micromoles per liter, multiply by 88.4; hemoglobin to grams per liter, multiply by 10.

[a] A complete definition list of all ERAS items was published in the protocol.[17] Unless otherwise indicated, data are expressed as number (percentage) of patients.

[b] Higher scores indicate severe preoperative systemic disease.

[c] Scores range from 1 to 9, with higher scores indicating higher level of vulnerability.

Outcome Data

A total of 680 patients (11.1%) experienced overall postoperative complications, and 352 (5.7%) experienced complications graded as moderate to severe (eFigure 1 in the Supplement). No differences were found in the number of patients with overall postoperative complications between the ERAS and non-ERAS groups (163 [10.2%] vs 517 [11.4%]; OR, 0.89; 95% CI, 0.74-1.07; *P* = .22) or in terms of readmission, reintervention, or survival (eFigure 1 in the Supplement). Fewer patients in the ERAS group had moderate to severe complications (73 [4.6%] vs 279 [6.1%]; OR, 0.74; 95% CI, 0.56-0.96; *P* = .02). eTables 4 and 5 in the Supplement show the stratified complications in THA and TKA in ERAS vs non-ERAS centers. In THA and TKA, the ERAS group had shorter median LOS (THA, 4 [IQR, 3-5] vs 5 [IQR, 4-6] days; TKA, 4 [IQR, 3-5] vs 5 [IQR, 4-6] days) (eFigure 1 and eTables 4 and 5 in the Supplement). Graduation of the severity of postoperative complications is shown in eTable 6 of the Supplement.

ERAS Adherence and Outcome Data

The overall adherence rate to the ERAS protocol components was 50.0% (IQR, 43.8%-62.5%), with the rate for ERAS facilities being 68.8% (IQR, 56.2%-81.2%) vs 50.0% (IQR, 37.5%-56.2%) at non-ERAS centers (*P* < .001). Adherence to specific ERAS items was greater in the ERAS group (Table 1). The ERAS group also had less bleeding (median blood loss, 200 [IQR, 100-400] vs 200 [IQR, 100-350] mL), less use of intraoperative crystalloids (median, 800 [IQR, 550-100] vs 1000 [IQR, 700-1200] mL), and greater intraoperative administration of tranexamic acid (1348 [85.9%] vs 3191 [70.2%]) (Table 1). In the TKA and THA procedures, adherence to perioperative ERAS items was greater in the ERAS group (eTables 7, 8, and 9 in the Supplement).

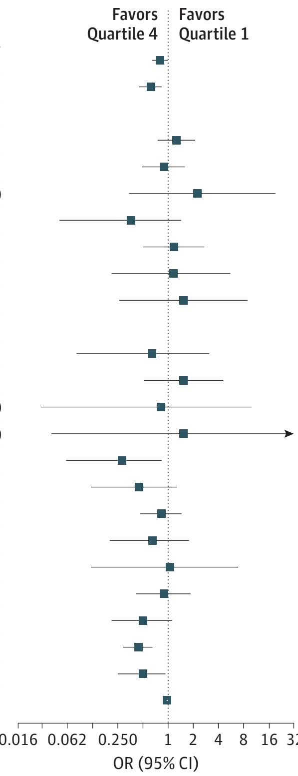
Patients in the ERAS group undergoing THA and TKA had less time to ambulation (mean [SD] for THA, 17.2 [13.3] vs 30.9 [24.4] hours; mean [SD] for TKA, 15.2 [13.9] vs 29.1 [15.5] hours) and oral intake (mean [SD] for THA, 6.04 [5.12] vs 8.12 [11.2] hours; mean [SD] for TKA, 6.05 [5.11] vs 8.20 [6.07] hours) (eTable 10 in the Supplement). Among the highest (quartile 4) and lowest (quartile 1) quartiles of adherence to ERAS items, quartile 4 also had a decrease in the rate of overall postoperative complications (270 [13.0%] vs 144 [10.6%]; OR, 0.80; 95% CI, 0.64-0.99; *P* < .001), moderate to severe postoperative complications (143 [6.9%] vs 59 [4.4%]; OR, 0.62; 95%, CI, 0.45-0.84; *P* < .001), postoperative hemorrhage (106 [5.1%] vs 31 [2.3%]; OR, 0.44; 95% CI, 0.29-0.65; *P* < .001), infection of uncertain source (17 [0.8%] vs 3 [0.2%]; OR, 0.28; 95% CI,0.06-0.84; *P* = .02), and surgical complications (37 [1.8%] vs 12 [0.9%]; OR, 0.50; 95% CI, 0.25-0.93; *P* = .03) (**Figure 2**). Gradation of the severity of postoperative complications is shown in eTable 11 in the Supplement. eFigures 2 and 3 in the Supplement show the results grouped by THA and TKA. In THA and TKA, the highest ERAS adherence group had shorter LOS (eFigures 2 and 3 in the Supplement) and less time to ambulation and oral intake (eFigure 4 in the Supplement) in THA and TKA (eFigures 5 and 6 in the Supplement).

Multivariable analysis of the associations with ERAS items showed a statistically significant reduction of complications in patients who had regional anesthesia (OR, 0.71; 95% CI, 0.53-0.96; *P* = .02) and early mobilization (OR, 0.61; 95% CI, 0.45-0.83; *P* = .002) (**Table 2**). A higher preoperative hemoglobin value (OR, 0.84; 95% CI, 0.77-0.91; *P* < .001) and tranexamic acid administration (OR, 0.66; 95% CI, 0.51-0.86; *P* = .002) were associated with fewer complications, whereas blood loss was associated with postoperative complications (OR, 1.00; 95% CI, 1.00-1.00; *P* < .001) (Table 2). In the multilevel study, early mobilization was associated with decreased complications (OR, 0.60; 95% CI, 0.42-0.86; *P* = .005) but not regional anesthesia (OR, 0.75; 95% CI, 0.54-1.05; *P* = .10) (Table 2).

Stratification of adherence to individual ERAS items by severity groups showed that healthier patients had higher adherence to ERAS (eTable 12 in the Supplement). In the ERAS centers, patients with ASA scores of I to II experienced less infection of uncertain source (1 [0.1%] vs 16 [0.5%]; OR, 0.19; 95% CI, 0.01-0.91; *P* = .04), less hemorrhage (18 [0.1%] vs 104 [3.2%]; OR, 0.45; 95% CI, 0.26-0.73; *P* = .001), and lower median LOS

Figure 2. Postoperative Outcomes and Enhanced Recovery After Surgery (ERAS) Adherence

Characteristics	Adherence Quartile[a] 1 (≤43.75%) (n = 2076)	2 (>43.75% to ≤50.00%) (n = 1079)	3 (>50.00% to 62.50%) (n = 1636)	4 (>62.50%) (n = 1355)	OR (95% CI)	P Value
Complications	270 (13.0)	116 (10.8)	150 (9.2)	144 (10.6)	0.80 (0.64-0.99)	.04
Moderate to severe complications	143 (6.9)	74 (6.9)	76 (4.6)	59 (4.4)	0.62 (0.45-0.84)	.002
Survival	2073 (99.9)	1079 (100)	1636 (100)	1355 (100)	–	–
Readmission	33 (1.6)	24 (2.2)	34 (2.1)	27 (2.0)	1.26 (0.75-2.11)	.38
Acute kidney injury	31 (1.5)	10 (0.9)	22 (1.3)	18 (1.3)	0.89 (0.49-1.59)	.70
Acute respiratory distress syndrome	2 (0.1)	0	0	3 (0.2)	2.25 (0.34-19.36)	.39
Pneumonia	9 (0.4)	2 (0.2)	2 (0.1)	2 (0.1)	0.36 (0.05-1.43)	.16
Arrhythmia	13 (0.6)	11 (1.0)	9 (0.6)	10 (0.7)	1.18 (0.50-2.72)	.69
Myocardial infarction	4 (0.2)	0	1 (0.1)	3 (0.2)	1.16 (0.21-5.57)	.85
Myocardial injury after noncardiac surgery	3 (0.1)	2 (0.2)	2 (0.2)	3 (0.2)	1.53 (0.26-8.93)	.62
Cardiac arrest	2 (0.1)	1 (0.1)	1 (0.1)	0	–	–
Pulmonary edema	5 (0.2)	4 (0.4)	2 (0.1)	2 (0.1)	0.64 (0.08-3.11)	.60
Deep vein thrombosis	7 (0.3)	5 (0.5)	3 (0.2)	7 (0.5)	1.53 (0.51-4.58)	.43
Pulmonary embolism	2 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)	0.82 (0.03-10.08)	.88
Stroke	1 (0.1)	0	1 (0.1)	1 (0.1)	1.53 (0.04-59.80)	.79
Infection of uncertain source	17 (0.8)	2 (0.2)	4 (0.2)	3 (0.2)	0.28 (0.06-0.84)	.02
Infection in bloodstream	14 (0.7)	6 (0.6)	12 (0.7)	4 (0.3)	0.45 (0.12-1.27)	.14
Surgical site infection (superficial)	35 (1.7)	18 (1.7)	27 (1.7)	19 (1.4)	0.83 (0.46-1.45)	.52
Surgical site infection (deep)	12 (0.6)	1 (0.1)	11 (0.7)	5 (0.4)	0.65 (0.20-1.78)	.41
Periprosthetic infection	3 (0.1)	0	8 (0.5)	2 (0.1)	1.05 (0.12-6.88)	.96
Urinary tract infection	19 (0.9)	8 (0.7)	11 (0.7)	11 (0.8)	0.89 (0.41-1.86)	.76
Paralytic ileus	24 (1.2)	9 (0.8)	8 (0.5)	8 (0.6)	0.51 (0.21-1.11)	.09
Postoperative hemorrhage	106 (5.1)	49 (4.5)	45 (2.8)	31 (2.3)	0.44 (0.29-0.65)	<.001
Surgical complications	37 (1.8)	9 (0.8)	21 (1.3)	12 (0.9)	0.50 (0.25-0.93)	.03
LOS, median (IQR), d	5 (4-6)	5 (3-6)	4 (3-6)	4 (3-5)	0.97 (0.96-0.99)	<.001



Patients are stratified by complications, type of complication, and other secondary outcomes and by quartile of adherence to the ERAS protocol. Surgical complications included all postoperative complications as defined by protocol[17] according to the standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions,[23] the standardized list, definitions, and the stratification developed by the Hip Society,[24] the standarized list and definitions of the Knee Society,[25] and the Standardized Bleeding Definitions for Cardiovascular Clinical Trials.[26] IQR indicates interquartile range; LOS; length of stay; and OR, odds ratio.

[a] Unless otherwise indicated, data are expressed as number (percentage) of patients.

(4 [IQR, 3-5] vs 5 [IQR, 3-6] days; OR, 0.95; 95% CI, 0.94-0.97; *P* < .001) compared with the non-ERAS centers (eFigure 7 in the Supplement), whereas patients with ASA scores of III to IV in the ERAS centers experienced less readmission compared with non-ERAS centers (18 [5.2%] vs 36 [28%]; OR, 1.90; 95% CI, 1.04-3.35; *P* = .04) (eFigure 8 in the Supplement). Regardless of belonging to a ERAS center or not, patients with ASA scores of I to II with greater adherence to ERAS had fewer moderate to severe complications (31 [3.0%] vs 79 [5.3%]; OR, 0.55; 95% CI, 0.35-0.83; *P* = .004) and lower median LOS (4 [IQR, 3-5] vs 5 [IQR, 4-6] days; OR, 0.97; 95% CI, 0.95-0.98; *P* < .001) compared with those with less adherence to ERAS (eFigure 9 in the Supplement), whereas no difference was found between patients with ASA scores of III to IV with more or less adherence to ERAS (eFigure 10 in the Supplement).

No significant association was found among the volume of patients recruited, hospital LOS, and postoperative complications. LOS decreased a mean of 0.0048 days due to an increase in 1 patient (*P* = .20, associated with β regression models), whereas the increase of 1 person per center increased the postoperative complications by 0.37% (*P* = .10, associated with β regression models) (**Figure 3** and eFigures 11-15 in the Supplement).

Median LOS was shorter in the ERAS group compared with the non-ERAS group (4 [IQR, 3-5] vs 5 [IQR, 4-6] days; *P* < .001). Regarding the difference by adherence quartiles, quartile 1 presented with a median LOS of 5 (IQR, 4-6) days, compared with 4 (IQR, 3-5) days in the highest adherence group (OR, 0.97; 95% CI, 0.96-0.99; *P* < .001) (Figure 3). The post hoc multivariable analysis of the influence of patient characteristics and ERAS items showed a statistically significant reduction of LOS in patients who achieved early mobilization (β coefficient, −0.51; 95% CI, −0.95 to −0.06; *P* = .03) and received local anesthesia (β coefficient, −1.59; 95% CI, −2.61 to −0.57; *P* = .002), whereas active prevention of unintentional hypothermia (β coefficient, 0.78; 95% CI, 0.30-1.26; *P* = .001), epidural anesthesia (β coefficient, 1.53; 95% CI, 0.79-2.26; *P* < .001), and complications (β coefficient, 2.63; 95% CI, 2.00-3.25; *P* < .001) were associated with an increase in LOS (eTable 13 in the Supplement). It was not necessary to censor any *P* value after the multiple comparison study to adjust the false discovery rate to 5%.

Table 2. Multivariable and Multilevel Analysis for Postoperative Complications[a]

Variable	No Complications	Complications	Univariable Analysis OR (95% CI)	Univariable Analysis P Value	Multivariable Analysis OR (95% CI)	Multivariable Analysis P Value	Multilevel Analysis OR (95% CI)	Multilevel Analysis P Value
Age, mean (SD), y	68.8 (10.2)	70.8 (10.5)	1.02 (1.01-1.03)	<.001	1.00 (0.99-1.02)	.46	1.00 (0.99-1.02)	.64
BMI, mean (SD)	30.1 (6.3)	30.0 (6.4)	1.00 (0.98-1.01)	.68	0.99 (0.97-1.01)	.35	0.99 (0.97-1.01)	.31
Frailty score, mean (SD)[b]	3.0 (1.0)	3.3 (1.1)	1.34 (1.25-1.44)	<.001	1.02 (0.89-1.16)	.75	1.04 (0.90-1.20)	.58
ASA classification[c]								
ASA I	360 (92.1)	31 (7.9)	NA	NA	NA	NA	NA	NA
ASA II	3765 (91.0)	371 (9.0)	1.14 (0.79-1.71)	.49	1.22 (0.66-2.47)	.56	1.26 (0.64-2.48)	.50
ASA III	1309 (83.1)	266 (16.9)	2.36 (1.62-3.55)	<.001	2.14 (1.11-4.50)	.03	2.23 (1.08-4.59)	.03
ASA IV	31 (72.1)	12 (27.9)	4.50 (2.04-9.47)	<.001	2.41 (0.68-8.02)	.16	3.07 (0.84-11.22)	.09
Diabetes	165 (82.1)	36 (17.9)	1.80 (1.22-2.57)	.002	1.10 (0.59-1.96)	.74	1.03 (0.55-1.95)	.924
Heart failure	122 (77.2)	36 (22.8)	2.45 (1.65-3.54)	<.001	1.35 (0.72-2.42)	.33	1.40 (0.74-2.63)	.30
Atrial fibrillation	344 (81.7)	77 (18.3)	1.90 (1.46-2.46)	<.001	1.30 (0.86-1.93)	.20	1.31 (0.86-2.00)	.22
Chronic kidney disease	273 (82.2)	59 (17.8)	1.81 (1.34-2.41)	<.001	1.19 (0.72-1.91)	.48	1.19 (0.71-1.99)	.50
Hemoglobin level, mean (SD), g/dL	14.1 (1.4)	13.6 (1.5)	0.79 (0.75-0.84)	<.001	0.84 (0.77-0.91)	<.001	0.83 (0.76-0.91)	<.001
Blood loss, mean (SD), mL	248.6 (213.7)	301.5 (263.6)	1.00 (1.00-1.00)	<.001	1.00 (1.00-1.00)	<.001	1.00 (1.00-1.00)	<.001
Tranexamic acid administration	4111 (90.6)	428 (9.4)	0.56 (0.47-0.66)	<.001	0.66 (0.51-0.86)	.002	0.75 (0.56-1.00)	.048
Presurgical education	1509 (89.4)	179 (10.6)	0.94 (0.78-1.12)	.49	1.38 (0.96-1.98)	.08	1.31 (0.85-2.02)	.22
Presurgical optimization	1078 (90.4)	115 (9.6)	0.94 (0.75-1.18)	.62	0.86 (0.62-1.20)	.39	0.94 (0.64-1.39)	.76
Preoperative fasting	2683 (89.5)	314 (10.5)	0.89 (0.76-1.04)	.15	1.07 (0.82-1.40)	.61	1.06 (0.76-1.47)	.73
Patient blood management	2144 (89.5)	252 (10.5)	0.92 (0.78-1.08)	.29	0.93 (0.71-1.23)	.63	0.85 (0.61-1.19)	.35
Preoperative carbohydrate drinks preload	110 (94.0)	7 (6.0)	0.51 (0.21-1.01)	.08	0.72 (0.24-1.70)	.49	0.44 (0.14-1.37)	.16
Avoidance of long-acting sedative premedication	2945 (88.9)	366 (11.1)	1.00 (0.85-1.17)	.97	1.03 (0.80-1.32)	.82	1.11 (0.83-1.47)	.49
Thromboprophylaxis	5023 (88.8)	632 (11.2)	1.15 (0.85-1.58)	.39	1.04 (0.68-1.67)	.86	1.14 (0.70-1.87)	.60
Regional anesthesia	4406 (89.6)	513 (10.4)	0.74 (0.61-0.89)	.001	0.71 (0.53-0.96)	.02	0.75 (0.54-1.05)	.10
PONV prophylaxis	3427 (89.2)	415 (10.8)	0.93 (0.79-1.10)	.39	0.93 (0.72-1.21)	.59	0.90 (0.67-1.21)	.47
Active prevention of unintentional hypothermia	4506 (88.7)	576 (11.3)	1.17 (0.94-1.47)	.16	1.54 (1.11-2.18)	.01	1.61 (1.05-2.46)	.03
Goal-directed fluid therapy	539 (91.2)	52 (8.8)	0.76 (0.56-1.01)	.07	0.98 (0.64-1.47)	.97	0.87 (0.54-1.40)	.57
Postoperative analgesia	5313 (88.9)	665 (11.1)	1.28 (0.77-2.28)	.37	2.40 (1.04-6.99)	.07	2.28 (0.84-6.16)	.11
Postoperative glycemic control	2849 (88.8)	359 (11.2)	1.03 (0.88-1.20)	.74	0.79 (0.61-1.02)	.07	0.91 (0.68-1.22)	.53
Early mobilization	1985 (91.6)	181 (8.4)	0.64 (0.53-0.76)	<.001	0.61 (0.45-0.83)	.002	0.60 (0.42-0.86)	.005
Early feeding	3536 (89.5)	417 (10.5)	0.86 (0.73-1.02)	.08	1.13 (0.86-1.48)	.38	1.15 (0.85-1.56)	.36
Analgesia								
Epidural anesthesia	342 (88.1)	46 (11.9)	1.09 (0.78-1.48)	.61	1.06 (0.67-1.64)	.79	0.95 (0.57-1.57)	.83
Regional anesthesia	836 (90.2)	91 (9.8)	0.86 (0.67-1.07)	.19	1.03 (0.71-1.45)	.88	0.91 (0.60-1.38,)	.67
Local anesthesia	230 (91.3)	22 (8.7)	0.76 (0.47-1.16)	.23	0.85 (0.36-1.72)	.76	1.05 (0.45-2.47)	.91

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by square of height in meters); IQR, interquartile range; NA, not applicable; OR, odds ratio; PONV, postoperative nausea and vomiting.

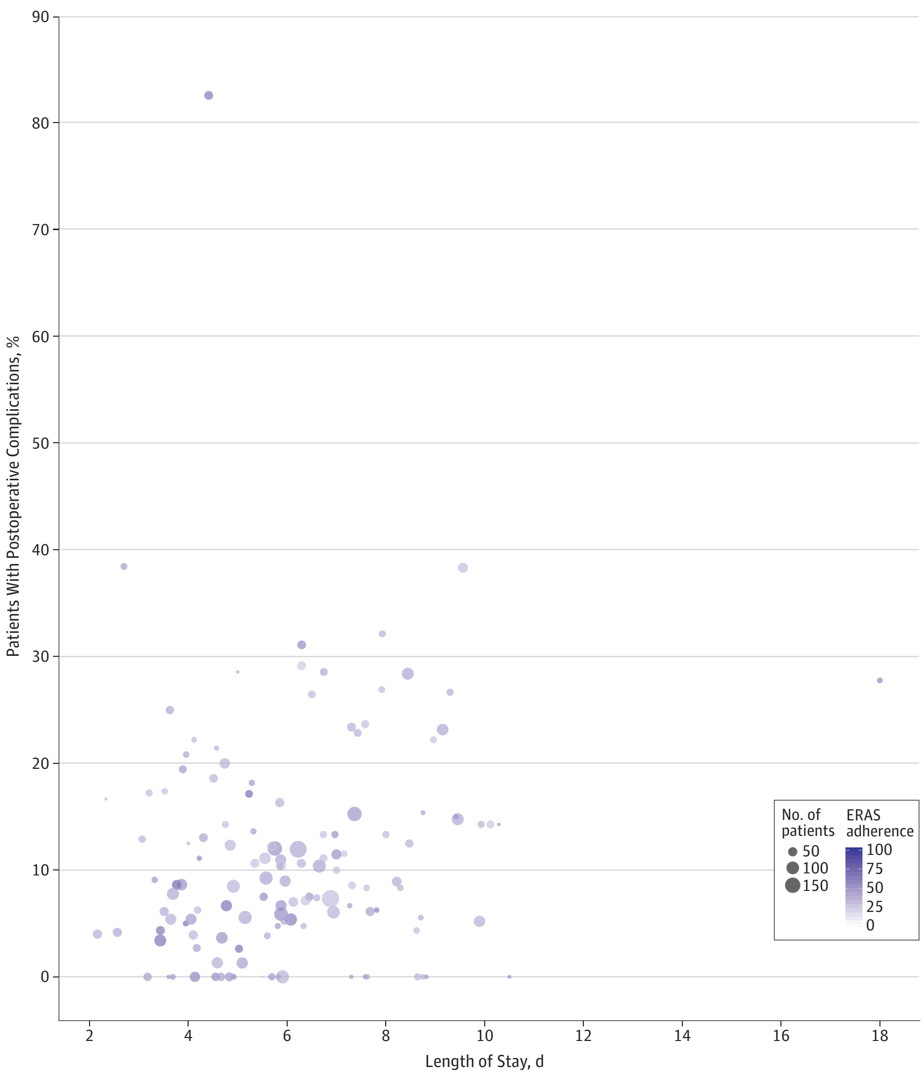
SI conversion factors: To convert albumin to grams per liter, multiply by 10; creatinine to micromoles per liter, multiply by 88.4; hemoglobin to grams per liter, multiply by 10.

[a] Statistically significant. Unless otherwise indicated, data are expressed as number (percentage) of patients.

[b] Scores range from 1 to 9, with higher scores indicating higher level of vulnerability.

[c] Higher scores indicate severe preoperative systemic disease.

Figure 3. Bubble Plot of the Rate of Postoperative Complications vs Length of Stay, Number of Participating Patients, and Rate of ERAS Program Adherence



For each hospital, the plot shows the mean percentage of adherence to the Enhanced Recovery After Surgery (ERAS) program (bubble color), the mean length of hospital stay, and percentage of patients who have postoperative complications. The bubble diameter indicates the number of patients that the hospital contributed to the study.

Discussion

POWER2 examined the postoperative outcomes in patients scheduled for THA or TKA and the outcomes associated with 16 evidence-based care components of an ERAS protocol in 131 centers in Spain and more than 6000 patients without limiting the inclusion of patients to centers with an established ERAS protocol. Results demonstrated that the implementation of an ERAS protocol was associated with improved postoperative outcomes.

A 2018 meta-analysis[27] found that ERAS protocols were associated with a significant decrease in transfusions, complication rates, and LOS without decreasing mortality or increasing the 30-day readmission rate in patients undergoing THA or TKA. During the last decade, the clinical pathways and care programs in THA and TKA have undergone considerable changes in many countries influenced by the ERAS concept.[28] However, in the absence of guidelines, the items that comprise these ERAS protocols were not clearly defined and present a great variability in the studies performed.[27] POWER2 found that the adherence to ERAS protocol in THA and TKA was low in all patients, although it was higher and close to 70% in self-proclaimed ERAS centers. The low adherence to ERAS protocols may be owing to the usual barriers to the implementation of ERAS in other disciplines, such as resistance to change, inadequate financing, lack of administration support, high turnover, poor documentation, and lack of time,[29] to which orthopedic procedures add the lack of guidelines and the economic pressure to achieve decreases in LOS.

An adherence of greater than 62.50% was associated with a decrease in postoperative complications, including mild and moderate to severe. Importantly, only some of the perioperative interventions seemed to be associated with a decrease in complications. Similarly, Khan et al[12] demonstrated that the application of an ERAS protocol based on a few components that included a multidisciplinary strategy involving patient education, multimodal analgesia, standardized perioperative anesthesia, local anesthetic infiltration, judicious fluid administration, tranexamic acid administration, and early mobilization led to a reduction in complications, LOS, and 30-day mortality. Khan et al[12] showed mean hospital stays of 3 days for patients in ERAS centers, whereas in POWER2, the best results were a median of 4 days in the patients with greater adherence to ERAS. Although some centers and health systems have stays of 3 or fewer days and even perform THA and TKA as outpatient procedures, the usual LOS[30] is similar to that reported in POWER2. This may be because, in Spain, patients are directly discharged home. In contrast, postacute care is typically available and covered by insurance companies in the United States and in other countries, making it easy for hospitals to discharge patients to rehabilitation facilities or to other intermediate centers.[31]

POWER2 found no association between comorbidities or frailty and complications, although patients with an ASA physical status score of III had more complications. We found that in the ERAS centers and in the group with greater ERAS adherence, there were more healthy patients. This finding could explain the best results in these groups. In fact, although the ERAS programs in THA and TKA have been proven safe and beneficial for most patients, we have found that in high-risk patients (ASA scores of III-IV), the application of ERAS, even in the highest adherence quartiles, did not result in better outcomes, although there were fewer readmissions.[12]

In patients undergoing major orthopedic surgical procedures, preoperative anemia, perioperative bleeding, and a liberal transfusion policy are the main risk factors for requiring an RBCT,[32] which increases complications and LOS.[33,34] Yang et al[35] showed that in patients undergoing TKA, tranexamic acid administration reduced blood loss and the need for RBCT. Similarly, we found that lower preoperative hemoglobin values and intraoperative bleeding were associated with an increase in complications, whereas the administration of tranexamic acid was associated with a decrease. Avoiding anemia, improving tolerance to anemia, and avoiding bleeding and RBCT are the pillars of patient blood management programs.[36] Surprisingly, the ERAS patient blood management item included in POWER2 has not been associated with better outcomes. In our opinion, many centers may apply the patient blood management measures without recognizing them as such.

It is not surprising that good analgesic control leads to early mobilization, and accomplishment of these items was associated with improved outcomes. Early mobilization in the first 24 hours after THA or TKA had been shown to be effective in reducing LOS, although it had not been associated with a decrease in complications.[37] Nevertheless, in POWER2, early mobilization was associated with fewer complications and shorter LOS. Conversely, epidural anesthesia was associated with a greater than 1-day increase in hospital LOS.

Early mobilization is considered a cornerstone in ERAS pathways and is strongly recommended as part of ERAS guidelines in many surgical disciplines.[8] ERAS Society guidelines recommend that patients be mobilized as soon as possible after surgery.[14] Chua et al[38] found that for patients undergoing THA, shorter time to mobilization was associated with hospital site and the absence of acute complications. For patients undergoing TKA, shorter time to mobilization was associated with hospital site and absence of donor blood transfusion.[38] These outcomes indicate that the patient who has complications cannot move early, and delays in mobilization could be taken as an alarm signal for possible complications. However, the delay until mobilization can also be related to the institution and local protocols, because certain hospitals encourage early patient mobilization, whereas others do not.

Strengths and Limitations

POWER2 had several strengths compared with other studies. This was a prospective study, with a case report form designed specifically for the study and with a short recruitment period of 2 months. We also included a large number of centers. Other studies have had years-long durations.[34] Khan et al[12] showed that the application of an ERAS program improved outcomes in a single center and in a long period of 7 years; the changes produced in such long periods decrease patient comparability. On the other hand, some of the studies with the highest number of cases were registers in national databases, in which it is assumed that all patients were treated with an ERAS protocol, but in which the adherence was not analyzed. We have included self-described ERAS centers and non-ERAS centers, and we have analyzed the variables that make up the ERAS protocol in all the centers, unlike the studies based on databases or the before-and-after studies. Moreover, the inclusion of consecutive, nonselected patients from 131 different centers without any selection bias increases the internal validity of our study. In addition, there were few losses of follow-up.

Our study has certain limitations. It was observational, which means that we can only obtain associations. Second, as previously mentioned, early mobilization can act as a confounding factor; because patients with complications could not fulfill this item, whether mobilization is an exposure factor or an outcome is debatable. We believe that it must be treated as both, and that all patients should be encouraged to move as soon as possible after surgery, because this has been shown to improve postoperative outcomes.[39] Third, we chose the individual ERAS items based on expert recommendations[15]; if we had selected other items, the results might be different. On the other hand, the patients in the ERAS group probably corresponded to more specialized centers and were healthier compared with patients in non-ERAS centers, which could explain why they had better outcomes.

Conclusions

This study found that ERAS protocols in THA and TKA do not appear to be applied in daily clinical practice, even in self-proclaimed ERAS centers, even though a greater adherence to ERAS improves postoperative outcomes. An effective pathway for THA and TKA consists of regional or local analgesia, anemia and bleeding management, and early mobilization as the basis of the care trajectory. Consequently, our findings suggest that the focus should be on these essential elements of care rather than on expanding adherence to the other, less evidence-based components in most ERAS protocols.

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