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Lessons Learned From the Global Orthopaedic Registry (GLORY): Study Design, Current Practice Patterns, and Future Directions
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Lessons from the Global Orthopaedic Registry

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Intended Audience:
This activity was developed for orthopedic surgeons.

Program Overview/Goal:
Patients undergoing orthopedic surgery are at high risk of surgery-related complications, including venous thromboembolism. In this supplement, the results of the Global Orthopaedic Registry are discussed, providing insight into global surgical and prophylaxis patterns as well as complications and outcomes following orthopedic surgery. Together, these articles add real-world data to the orthopedic surgery literature and will allow physicians to assess the impact of different surgical choices.

Agenda:
Overview of the Global Orthopaedic Registry (GLORY)
Orthopedic Practice in Total Hip Arthroplasty and Total Knee Arthroplasty: Results From the Global Orthopaedic Registry (GLORY)
Practice Patterns in the Use of Venous Thromboembolism Prophylaxis After Total Joint Arthroplasty—Insights From the Multinational Global Orthopaedic Registry (GLORY)
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Educational Objectives:
At the end of the Lessons from the Global Orthopaedic Registry, participants will be able to:
Explain global surgical practice patterns in orthopedic surgery.
Describe prevalent global prophylaxis regimens currently used in orthopedic surgery.
Recognize how these different practice patterns can influence clinical outcomes in orthopedic surgery.
Identify best practice when designing and running a registry.
Use best-practice guidelines to help make informed clinical decisions in orthopedic surgery.

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Lessons From the Global Orthopaedic Registry (GLORY)

2 **Overview of the Global Orthopaedic Registry (GLORY)**
Frederick A. Anderson, Jr., PhD

5 **Orthopedic Practice in Total Hip Arthroplasty and Total Knee Arthroplasty: Results From the Global Orthopaedic Registry (GLORY)**
James Waddell, MD, Kirk Johnson, MD, Werner Hein, MD, Jens Raabe, MD, Gordon FitzGerald, PhD, and Flávio Turibio, MD

14 **Practice Patterns in the Use of Venous Thromboembolism Prophylaxis After Total Joint Arthroplasty—Insights From the Multinational Global Orthopaedic Registry (GLORY)**
Richard J. Friedman, MD, FRCSC, Alexander Gallus, MBBS, FRACP, FRCPA, FRCP(C), Enrique Gil-Garay, MD, PhD, Gordon FitzGerald, PhD, and Fred Cushner, MD

22 **Complications and Functional Outcomes After Total Hip Arthroplasty and Total Knee Arthroplasty: Results From the Global Orthopaedic Registry (GLORY)**
Fred Cushner, MD, Giancarlo Agnelli, MD, Gordon FitzGerald, PhD, and David Warwick, MD, FRCS (Orth)

29 **Lessons Learned From the Global Orthopaedic Registry (GLORY): Study Design, Current Practice Patterns, and Future Directions**
David Warwick, MD, FRCS (Orth), Giancarlo Agnelli, MD, Fred Cushner, MD, Richard J. Friedman, MD, FRCSC, Gordon FitzGerald, PhD, and Alexander Gallus, MBBS, FRACP, FRCPA, FRCP(C); and the GLORY Publication Committee

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Overview of the Global Orthopaedic Registry (GLORY)

Frederick A. Anderson, Jr., PhD

The Global Orthopaedic Registry (GLORY) is an international registry of patients who underwent elective primary total hip arthroplasty (THA) or primary total knee arthroplasty (TKA) during the years 2000 through 2004. By providing a real-world view of practices and outcomes, its objectives are to compare practice with evidence-based standards, to identify where such standards do not exist but are needed, and ultimately to lead to hypotheses for improving research, education, and patient care that can be verified by controlled clinical trials.

Previous data on outcomes after THA or TKA have been collected from clinical trials that assess individual devices or from country-specific registries. The Swedish THA and TKA registries were among the first total joint registries established.[1,2] A variety of country-specific registries have provided important information on both short- and long-term outcomes following THA and TKA. However, a majority of countries do not have well-established national joint arthroplasty registry programs, and both established registries and clinical trials have limitations.

Firstly, clinical trials generally assess a newly developed implant, and most registries focus on outcomes resulting from different types of implant and the factors that affect implant survival. As a result, they provide a valuable quality-improvement tool to identify superior and inferior implants at an early point following their introduction into clinical practice.[1,3] However, they offer relatively little information about a wide range of surgical practices, postoperative complications, and functional outcomes. GLORY was designed to monitor a broad range of practices, complications, and outcomes. This approach distinguishes this registry from previous efforts directed solely at assessing implant survival.[4]

Secondly, most registries and clinical trials gather data from a single country, or even from a single hospital. As a multinational registry, GLORY includes global, rather than solely country-specific, hospital-specific, or implant-specific, data. GLORY can thus provide unique insight into the geographical differences in THA and TKA practices and also clinically valuable data on the prevalence of postoperative complications.

This voluntary registry is physician directed and came into being by the merger of 2 preexisting registries, the International Orthopaedic Registry (IOR) and The Hip and Knee Registry (THKR), which was restricted to North America (Figure 1). THKR enrolled patients from 1995 to 2002. Results from the THKR have been published previously.[5] THKR enrolled over 40,000 total joint procedures from more than 500 surgeons in the United States and Canada. However, its follow-up rate was only about 30%, raising concerns about the possibility of bias in the reporting of complications. In 2001 the IOR was formed and merged in 2002 with the THKR to form GLORY. The IOR case report included all variables later contained in GLORY, while the THKR only included 80% of these variables. This makes GLORY more detailed than the THKR and similar to the IOR.

"GLORY was designed to monitor a broad range of practices, complications, and outcomes."

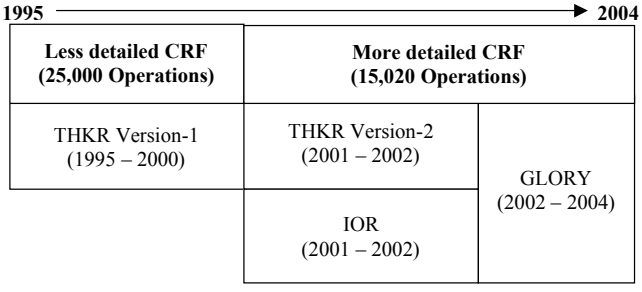

Figure 1. Understanding the evolution of The Hip and Knee Registry (THKR), International Orthopaedic Registry (IOR), and Global Orthopaedic Registry (GLORY) data sets. THKR was limited to North America–based orthopedic surgical practices. IOR included surgeons practicing outside of North America. Abbreviation: CRF, case report form.

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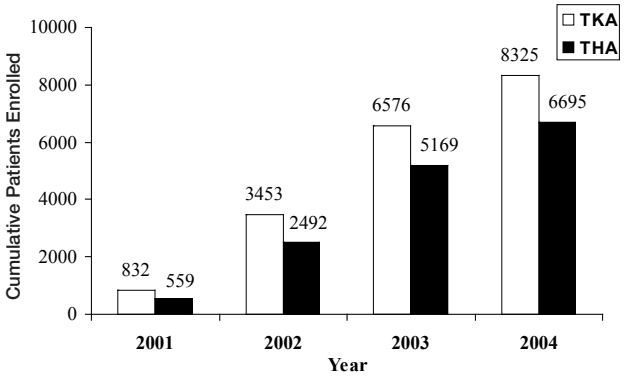

Figure 2. Cumulative patient enrollment by year. Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty.

Study Design

GLORY was designed and coordinated by the Center of Outcomes Research (University of Massachusetts, USA). The registry is governed by the GLORY Scientific Advisory Board, which includes orthopedic surgeons representing each participating country and clinical scientists with experience in the design and analysis of registry data from joint arthroplasty patients.

Participating surgeons enrolled consecutive patients ≥18 years of age who had undergone elective primary THA or TKA. In-hospital data were collected on all patients. Wherever possible, patients were followed up at approximately 3 months and again at 12 months to collect data on selected aspects of their outpatient management and post-discharge functional outcomes. In contrast to a clinical trial, there is no imposed experimental intervention. Patient treatment is determined solely by the physicians.

One hundred hospitals participated in 13 countries worldwide: Australia, Brazil, Bulgaria, Canada, Colombia, Germany, Italy, Japan, Poland, Spain, Turkey, United Kingdom (UK), and the United States (USA). Surgeons were asked to enroll the first 10 cases of THA and the first 10 cases of TKA they see each month. For smaller centers this meant enrolling all patients who met entry criteria, while for larger centers this was an unbiased method for selecting a patient sample. The registry enrolled 15,020 patients who underwent primary elective unilateral total hip (6,695 patients) or knee replacement surgery (8,325 patients) between June 2001 and December 2004 (Figures 2 and 3). Of these patients 70% (10,490) completed either a 3-month (5,346) or 12-month follow-up (1,320) only, or both (3,824).

The scientific coordinating center ensures that the registry complies with scientific and ethical standards. Each hospital involved in GLORY received ethics committee or institutional review board approval, and, where mandated by their ethics committee, participating surgeons obtained informed consent from patients prior to their participation in the registry and for follow-up contact after discharge.

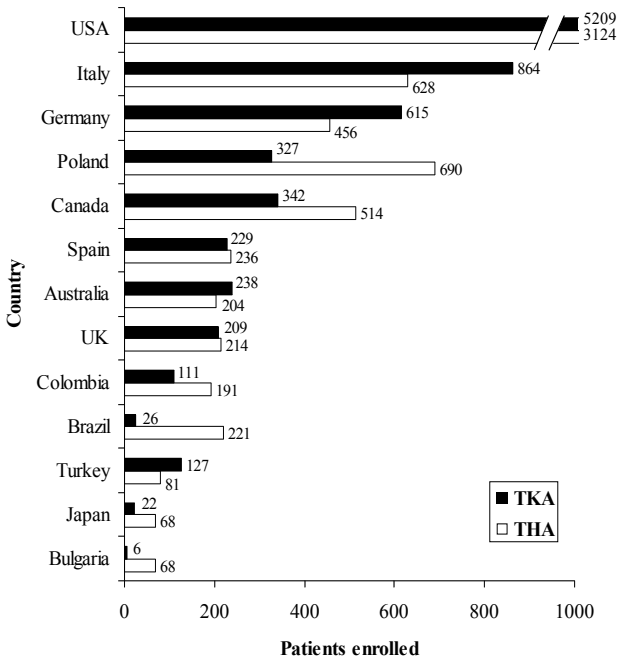

Figure 3. Patient enrollment by country. Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty.

Data Collection

Participating surgeons or trained study coordinators collected data on standardized case report forms. Data include patient demographics, primary diagnosis, preexisting comorbid conditions, length of hospital stay, type of anesthesia, prophylaxis for venous thromboembolism (including type and duration), in-hospital complications, discharge disposition, and patient self-reported quality of life. The completed case report forms were then sent to the scientific coordinating center for entry into the database and for analysis. Data were entered into a computer database and subsequently analyzed using a Statistical Analysis System (SAS)-PC. Data quality control was monitored using standardized query logic. Out-of-range or illogical responses were queried to the surgeon on a quarterly basis. Corrections were faxed to the scientific coordinating center.

Key outcomes include clinically recognized venous thromboembolism (VTE), postoperative bleeding, wound infection, dislocation, functional status, and death. A deep vein thrombosis (DVT) or pulmonary embolism (PE) is defined as a symptomatic event that was subsequently confirmed by diagnostic imaging techniques such as venography, ultrasound, radioisotope scanning, and 3D computed tomography scanning. Clinically important bleeding following THA/TKA is defined as "Bleeding that is recorded by the surgeon as being outside the range of typical expected levels of bleeding following THA/TKA, or bleeding that is cited as the cause of prolonged hospital stay." Functional status was assessed through a quality-of-life self-assessment questionnaire consisting of the Short Form-8 Survey (SF-8) and the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index, completed by the patients prior to hospitalization and again at each follow-up.

Strengths of GLORY

GLORY monitors practice trends and clinical outcomes in unselected patients in a real-world routine patient care environment. These data may be more representative than data collected in the context of controlled clinical trials, in which restrictive inclusion/exclusion criteria may limit generalizability. GLORY is the only multinational orthopedic registry using standard data collection instruments, definitions, and patient selection criteria across many different healthcare systems. By monitoring what physicians are doing in the "real world," the adoption of evidence-based practice standards can be assessed, and strategies identified to improve the quality and value of health care. Furthermore, data from GLORY can serve to plan educational programs and as a hypothesis-generating tool to plan controlled clinical trials.

Limitations of GLORY

GLORY is a voluntary registry, and as such, it is likely that many of the surgeons who agreed to provide registry data already pay special interest to evidence-based practice standards. Indeed, some differences are found in the multinational prophylaxis practices reported in this supplement compared with previous US-specific studies of orthopedic surgeons.[6] While this may result in an overestimation of the adoption of such standards, the database nevertheless provides insights into current everyday practice and its regional variations, and it allows an appraisal of contemporary compliance with international guidelines and recommendations. As GLORY is a large-scale voluntary registry, no hospital audits were performed to check data quality. Data quality control was ensured through standardized query logic; out-of-range or illogical responses were queried to the surgeon on a quarterly basis. A voluntary registry is not a substitute for randomized clinical trials and therefore of limited value in determining the safety or efficacy of different treatment options.

GLORY Results

In this supplement, findings from GLORY will be presented and placed within the context of current knowledge regarding THA and TKA in 3 articles, dealing with orthopedic practices, thromboprophylaxis practices, and complications and outcomes consecutively. The lessons that can be learned from GLORY regarding study design and current practice patterns will be discussed in the epilogue, and future directions explored.

Author's Disclosure Statement and Acknowledgments

GLORY is supported by an unrestricted educational grant from sanofi-aventis to the Center for Outcomes Research at the University of Massachusetts Medical School, Worcester, Massachusetts. The registry is overseen by an independent Scientific Advisory Committee. Additional information about this registry, including a full list of the Advisory Committee members, is available on the website at www.outcomes.org.

Dr. Anderson is a consultant for sanofi-aventis, GlaxoSmithKline, and Ortho McNeill.

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APPENDIX

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Orthopedic Practice in Total Hip Arthroplasty and Total Knee Arthroplasty: Results From the Global Orthopaedic Registry (GLORY)

James Waddell, MD, Kirk Johnson, MD, Werner Hein, MD, Jens Raabe, MD, Gordon FitzGerald, PhD, and Flávio Turibio, MD

Abstract

The Global Orthopaedic Registry (GLORY) offers global and country-specific insights into the management of patients undergoing total hip arthroplasty and total knee arthroplasty by drawing on data, from June 2001 to December 2004, of 15,020 patients in 13 countries. GLORY achieved a 70% follow-up rate at 3 and/or 12 months, allowing longer-term findings to be reported.

This paper reports data from GLORY on patient demographics, surgical approaches to patient management, selection of implants, anesthetic and analgesic practices, blood management, length of hospital stay, and patient disposition at discharge. Some aspects of orthopedic practice differ between countries. There was notable variation in the choice and selection of prosthesis, fixation of implants, length of hospital stay, and discharge disposition.

The Global Orthopaedic Registry (GLORY) is an international registry created to examine practices and outcomes in patients who undergo elective total hip arthroplasty (THA) or total knee arthroplasty (TKA). This voluntary registry is physician-directed and came into being by the merger of 2 preexisting registries, the International Orthopaedic Registry (IOR) and The Hip and Knee Registry (THKR), which was restricted to North America. Results from THKR have been published previously; they highlighted the challenges orthopedic surgeons face when aiming to meet the goal of minimizing hospital stay while ensuring the best long-term outcomes.[1]

With the creation of GLORY, it has been possible to gather data on 15,020 patients from 13 countries (see also Anderson[2] in this supplement for details of the study).

The contemporary literature on orthopedic practice suggests significant variation both between countries and between hospitals. Orthopedic surgeons have a wide and ever-changing choice of implants for use in surgery and are encouraged to adopt best-practice guidelines on many aspects of patient care. Surveys suggest tremendous worldwide variation in both the availability and the cost of different implants for use in THA and TKA.[3,4] Internationally, there are considerable differences between countries in the use of technologies employed to minimize blood transfusion during orthopedic surgery,[5] and even within given countries and regions, orthopedic practices can vary greatly according to the preferences and opinions of operating surgeons.[6,7] For example, while all orthopedic surgeons in the United States appear to agree on the need for prophylaxis against venous thromboembolism (VTE) in patients undergoing THA and TKA, the chosen methods and duration of prophylaxis are highly variable according to individual practices and preferences.[8]

GLORY allows for further study of the similarities and differences in orthopedic practice between countries. This paper reports the registry findings on patient demographics, which highlight parallels and differences between countries in terms of the surgical approaches to patient management, selection of implants, anesthetic and analgesic practices, blood management, length of hospital stay, and patient disposition at discharge. The results presented here are complemented by the GLORY data described in other articles in this supplement, which focus on VTE-prophylaxis patterns[9] and the functional outcome and complication rates observed following TKA and THA.[10] As with other GLORY data sets, the findings regarding orthopedic practice allow a contrast to be made between prevailing practices in the United States and those adopted in other participating countries. This

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Table I. Demographics of Patients Undergoing Total Hip Arthroplasty

Demographic (%)	Countries		
	All	USA	Others
Patients, n	6,695	3,124	3,571
Median age, years (IQR)	68 (57–75)	69 (58–76)	67 (56–73)
Women	59	55	61
Median BMI, kg/m^2 (IQR)	27 (25–31)	28 (25–33)	27 (24–30)
Obese (BMI >30 kg/m^2)	31	38	25
Health problem with ASA grade of severe or worse	27	31	23
Primary diagnosis			
Osteoarthritis	83	86	80
Rheumatoid arthritis	3	2	4
Osteonecrosis	7	6	8
Other	7	7	8
Prior contralateral THA	18	17	19
Location of other disabling joint disease			
None	50	49	51
Contralateral hip	25	21	29
Contralateral knee	8	6	9
Back	16	18	14
Ipsilateral knee	9	8	11
Upper extremity	3	3	4
Foot/ankle	2	2	3
Other	3	3	2
Previous surgery on index joint			
None	91	95	87
Femoral osteotomy	1.0	0.2	1.6
Acetabular femoral fixation	0.2	0.1	0.4
Pelvic osteotomy	0.6	0.1	1.0
Hip arthroplasty	2.3	1.5	3.0
Proximal femoral fixation	1.1	0.8	1.5
Femoral head fixation	0.4	0.3	0.5
Other	4.8	2.5	6.8

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; IQR, interquartile range; THA, total hip arthroplasty.

contrast is valid based upon the number of participating countries and centers. However, data from individual countries other than the United States may sometimes be more reflective of center practice, because there were relatively few centers in some countries.

Methods

The methodology of data collection for GLORY is described in detail in the opening article in this supplement.[2] The registry enrolled 15,020 patients from 100 hospitals in 13 countries (Australia, Brazil, Bulgaria, Canada, Colombia, Germany, Italy, Japan, Poland, Spain, Turkey, United Kingdom, United States) during the period June 2001 to December 2004. Patients eligible for GLORY were those undergoing THA or TKA for whom a 12-month clinical follow-up period was feasible. GLORY had a 70% combined 3-month and/or 12-month follow-up rate.

Data concerning patient demographics, primary diagnosis, preexisting comorbid conditions, surgical approach, implant selection, blood management, type of anesthesia, VTE prophylaxis, length of hospital stay, and discharge disposition were gathered using standard case report forms (CRFs). Where appropriate, chi-square or Fisher's exact tests were used to test for rate differences in different groups. Wilcoxon's rank sum test was used to test differences between continuous variables, by group.

Results

Total Hip Arthroplasty

Demographic Data on Total Hip Arthroplasty. Data were provided on 6,695 THA procedures by 86 of the 100 participating hospitals (Table I). The median age of patients undergoing this procedure in the United States was 69 years, and for other participating countries was 67 years. More women than men underwent THA in both the United States and other countries (55% and 61% of patients were women, respectively). The median body mass index (BMI) of THA patients was similar in the United States (28 kg/m^2) and other countries (27 kg/m^2), although more patients from the United States had a BMI > 30 kg/m^2 (38%) compared with other countries (25%).

In terms of coexisting chronic health problems, 31% of US patients, as compared with 23% of patients from other countries, had severe or worse chronic health problems of moderate to significant severity (ASA [American Society of Anesthesiologists] Grade III or above). As expected in these orthopedic patients, a high proportion (86% of patients in the United States and 80% in other countries) suffered from osteoarthritis. A smaller proportion of THA patients (2% in the United States and 4% in other countries) had rheumatoid (inflammatory) arthritis or were diagnosed with osteonecrosis (6% of patients in the United States and 8% in other countries) (Table I).

Table II. Procedure Used for Total Hip Arthroplasty

Procedure, %	Countries		
	All	USA	Others
Surgical approach			
Posterior	55	73	43
Trochanteric	11	5	15
Anterior lateral	33	22	41
Duration of surgery <2 hours	81	77	82
Anesthesia*			
General	51	58	45
Spinal	41	33	47
Epidural	14	18	11
Lumbar plexus block	2	0.1	4
Continuous epidural analgesia	16	22	12
VTE prophylaxis			
Any in-hospital	99.5	99	99.6
Any post-discharge	29	44	19
Antibiotics			
Single dose	9	0.5	16
≤24 hours	44	54	35
>24 hours	47	45	48
Heterotopic ossification prophylaxis			
None	82	96	74
Radiation	1	2	0.2
Indomethacin	17	2	26

*Patients could receive more than one type of anesthetic.
Abbreviations: VTE, venous thromboembolism.

Of patients enrolled in GLORY, 18% had undergone a prior contralateral THA. Half the patients had significant arthritic problems in other joints that were considered likely to influence the outcome of THA; 25% presented with contralateral hip arthritis, 9% with ipsilateral knee arthritis, and 8% with contralateral knee arthritis. Ninety-five percent of US patients had not had a previous operation to the joint, 0.2% had undergone a previous femoral osteotomy, 0.1% a previous pelvic osteotomy, 0.8% a proximal femoral fixation, and 1.5% a unipolar or bipolar arthroplasty for fracture. Patients from the UK GLORY centers had only a 2% incidence of previous surgery, while in the Australian center, 66% of patients had undergone previous hip surgery.

The basic demographic findings of THA patients in GLORY reflect the reports of other orthopedic registries and large-scale studies in orthopedic patients. Candidates for THA are more likely to be women between 65 and 70 years of age with a history of osteoarthritis without previous orthopedic surgery.[11-16]

Procedure Used for Total Hip Arthroplasty. Total population data from GLORY show that 55% of procedures were performed using a posterior approach, 33% using an anterior lateral approach, and 11% using a trochanteric approach (Table II). Results reveal substantial variation in surgical approach by country. In the United States, 73% of patients were operated upon via a posterior approach. There was no association between the type of approach and dislocation rate in the United States, yet a significant association was seen ($P = .002$) in other participating countries; the highest dislocation rates were noted for THA using a posterior approach (2.1%), followed by a 1.6% dislocation rate using a trochanteric approach, and only 0.5% using an anterior lateral approach.

Most procedures (81%) were completed within 2 hours. Length of surgery was not significantly associated with the rates of in-hospital or post-discharge complications in the United States, although in other participating countries, an association was noted between length of surgery and both dislocation rates ($P = .04$) and fracture rates ($P = .002$). Indeed, when duration of surgery extended beyond 2 hours, dislocation rates and fracture rates were higher compared with rates for surgery of 2 hours or less: 2.3% versus 1.1% dislocation and 2.5% versus 0.8% fracture, respectively.

General anesthesia was the preferred choice of anesthesia—being used in 51% of THA patients in GLORY—followed by spinal anesthesia (41% of cases) and epidural anesthesia (14% of cases). Combined forms of anesthesia were employed for some patients (Table II). Continuous epidural catheter delivery of analgesia was used in 16% of THA patients; in most of these cases (97%), this pain relief was discontinued after the second postoperative day.

Blood salvage is a technique where blood lost by the patient during the surgery is collected and transfused back into the patient either intraoperatively or postoperatively. In GLORY, only 18% of THA patients were managed using blood-salvage techniques, of which approximately one half received intraoperative blood salvage (Table III). A quarter (25%) of THA patients received autologous blood postoperatively at a median volume of 600 mL, and 57% of patients required 1 or more unit of blood (median volume, 600 mL) following surgery (Table III).

As described in detail by Friedman and colleagues,[9,17] 99.5% of GLORY patients undergoing THA were given in-hospital VTE prophylaxis. Prophylaxis was continued after discharge in only 29% of patients (Table II). Antibiotic therapy was given for > 24 hours to 47% of patients, whereas 44% of subjects received antibiotics for ≤ 24 hours and 9% received a single dose after THA. Only 18% of all patients were given specific therapy for the prevention of heterotopic ossification, although this practice was common in the German center. Indomethacin was the treatment of choice for prophylaxis against ossification.

Table III. Blood Usage in Total Hip Arthroplasty Patients

	Countries		
	All	USA	Others
Preoperative autologous blood management, %	25	42	15
Blood salvage, n	4,459	1,657	2,802
Total, %	18	22	15
Intraoperative, %	1	2	1
Postoperative, %	9	6	10
Both, %	8	15	4
Blood transfusion*, n	5,149	1,778	3,371
Total, %	57	55	58
Autologous, %	25	38	18
Donor, %	36	21	44

*Patients could receive more than 1 type of transfusion.

Table IV. Selection of Total Hip Arthroplasty Implants

Implant	Countries		
	All	USA	Others
Patients, n	6,695	3,124	3,571
Acetabular component			
Fixation, %			
Cemented	18	5	29
Porous	55	76	38
Hydroxyapatite	18	12	23
Other	8	6	9
Bearing surface			
Standard polyethylene	36	28	42
Highly cross-linked polyethylene	55	63	49
Metal	5	5	5
Ceramic	4	3	4
Other	0.2	0.1	0.3
Femoral component			
Fixation (stem)			
Cemented	41	30	50
Porous	41	55	29
Hydroxyapatite	16	14	18
Other	2	1	3
Head material			
Steel	19	4	32
Chrome	57	82	36
Titanium	9	7	10
Ceramic	12	5	18
Other	3	1	4

Table V. Length of Hospital Stay and Discharge Disposition After Total Hip Arthroplasty

Country	Patients, n	Median Length of Hospital Stay, Days (IQR)	Discharge, %	
			Home	Rehab. Center /Other
All	6,695	5 (3–11)	64	36
Australia	204	6 (5–8)	63	37
Brazil	221	7 (6–7)	97	3
Bulgaria	68	19 (16–23)	97	3
Canada	514	5 (4–6)	31	69
Colombia	191	4 (3–5)	98	2
Germany	456	11 (9–13)	70	30
Italy	628	10 (9–12)	88	12
Japan	68	30 (29–32)	19	81
Poland	690	16 (14–21)	94	6
Spain	236	12 (9–14)	100	0
Turkey	81	11 (8–16)	100	0
UK	214	9 (8–10)	97	3
USA	3,124	3 (3–4)	47	53

Abbreviations: IQR, interquartile range.

Implant Selection for Total Hip Arthroplasty. Analyses of all data from GLORY showed that 18% of THA patients received a cemented acetabular component, 55% received an uncemented component (uncemented metal shell with polyethylene liner), and 18% received a hydroxyapatite-coated metal shell with a polyethylene liner (Table IV). Choice of polyethylene was varied. In 36% of patients undergoing THA, standard polyethylene was used, but in 55% highly cross-linked polyethylene was employed. In the United States highly cross-linked polyethylene was used more often than standard polyethylene (63% and 28%, respectively), while these types of polyethylene were used more evenly in other participating countries (49% and 42%, respectively). Overall, 5% of THAs were metal on metal and 4% were ceramic on ceramic.

Geographic differences were also seen in cementing practices, with only 5% of US cups being cemented, compared with 29% of cups in other participating countries. In the United States, porous cups were used most frequently (76%); in the other participating countries, porous cups were used in 38% of THA patients.

Overall, there was equal division between cemented (41%) and porous (41%) in-growth femoral components, and there was a 16% use of hydroxyapatite-coated components (Table IV). Cemented femoral stems were used more often in participating centers outside of the United States (50%) than in the US centers (30%).

One of the most important concerns following THA is the durability of joint replacements. The available long-term evidence suggests excellent clinical success rates and high 15- to 20-year survivorship of femoral and acetabular components, whether cemented or fixed by cementless means.[18,19] However, there are recognized advantages and disadvantages to both cemented and cementless fixation.[20,21] Increasingly, cementless acetabular socket fixation is viewed as best practice for THA, with cemented fixation becoming almost obsolete.[22-24] The GLORY data appear to reflect this trend away from widespread reliance on cemented acetabular components.

The use of cementless femoral fixation is more controversial than cementless acetabular fixation. Indeed, closer scrutiny of the literature reveals that some follow-up and survival studies appear to favor cementless femoral components,[11,25,26] some advocate cemented femoral fixation,[27] while others report no clear differences between the 2 forms of fixation.[28,29] Differences in surgical technique, prosthesis design, and factors such as differing patient characteristics and follow-up time between studies could have contributed to these conflicting reports. In general, the GLORY data show low usage of cemented femoral components, although cement is still used more often in femoral fixation than in acetabular fixation. Of note, the practice of cementless fixation in THA was more common in the United States than in other participating countries.

Concerns have arisen about the wear of polyethylene in cementless prosthetic components, which is thought to lead to osteolysis and loosening of the implant and appears to particularly affect acetabular components.[30,31] Increased wear of acetabular cementless cups has been reported in a 15-year follow-up study comparing cemented and cementless cup fixation,[23] and this has been corroborated by other studies.[11,32]

Postoperative Management of Total Hip Arthroplasty Patients. Following THA, 64% of GLORY patients were discharged from hospital to their home, while 36% were discharged to a rehabilitation or other facility (Table V). Physical therapy was provided to 73% of patients after their discharge from the acute hospital setting.

Table VI. Demographics of Patients Undergoing Total Knee Arthroplasty

Demographic, %	Countries All	USA	Others
Patients, n	8,325	5,209	3,116
Median age, years (IQR)	70 (62–76)	69 (61–76)	71 (65–76)
Women	66	62	72
Median BMI, kg/m^2 (IQR)	30 (27–35)	31 (27–36)	29 (26–33)
Obese (BMI >30 kg/m^2)	50	56	42
ASA grade severe or worse	32	37	24
Primary diagnosis			
Osteoarthritis	94	95	91
Rheumatoid arthritis	3	2	5
Osteonecrosis	0.5	0.5	0.5
Other	3	2	3
Prior contralateral TKA	20	19	21
Location of other disabling joint disease			
None	46	48	42
Contralateral knee	36	32	42
Contralateral hip	4	3	7
Back	12	11	13
Ipsilateral hip	4	3	6
Upper extremity	4	3	6
Foot/ankle	3	3	4
Other	3	4	3
Previous surgery on index joint			
None	70	69	73
Patellectomy	0.3	0.3	0.1
High tibial osteotomy	1.5	0.9	2.5
Distal femoral osteotomy	0.1	0.1	0.1
ORIF femur	0.4	0.5	0.1
ORIF tibia	0.5	0.6	0.5
Open meniscectomy	7	8	4
Arthroscopy	10	10	9
Ligament reconstruction	1	1	0.6
Patellofemoral alignment	0.4	0.4	0.3
Other	8	6	13
Alignment			
Normal	18	16	21
Varus deformity	62	60	65
Valgus deformity	20	24	14

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; IQR, interquartile range; ORIF, open reduction with internal fixation; TKA, total knee arthroplasty.

Table VII. Procedure Used for Total Knee Arthroplasty

Procedure, %	Countries All	USA	Others
Surgical approach			
Anteromedial	88	87	91
Anterolateral	1	1	1
Subvastus	6	7	4
Other	5	5	4
Duration of surgery <2 hours	86	88	85
Anesthesia*			
General	43	43	42
Spinal	46	43	52
Epidural	20	25	12
Lumbar plexus block	1	0.02	2
Anterior continuous catheter	0.2	0	0.6
Femoral nerve block	5	5	4
Continuous epidural analgesia	25	31	17
VTE prophylaxis			
Any in-hospital	99	99	99
Any post-discharge	36	45	23
Antibiotics			
Single dose	10	0.6	26
≤24 hours	44	49	35
>24 hours	46	51	39

*Patients could receive more than 1 type of anesthetic.
Abbreviations: VTE, venous thromboembolism.

Once again, patterns of postoperative management showed marked geographic variation. While 97% of patients from the participating UK centers (with a median hospital stay of 9 days) and 98% of Colombian patients were discharged home (median hospital stay of 4 days), only 47% of patients in the United States (median stay of 3 days) and 31% of Canadian patients (median stay of 5 days) went back to their own home. There was an overall trend toward increased length of acute hospital stay in those jurisdictions where patients were not routinely discharged to rehabilitation or where post-acute hospital-based rehabilitation could not be offered. Thus, the median hospital stay for THA patients in GLORY was 7 days for those discharged to home and was 4 days for those discharged to rehabilitation or some other facility. The differences in length of stay should, however, be treated with caution, as differences in the percentage of patients discharged to rehabilitation facilities, where the care is essentially equivalent to the hospital, may have an effect on the mean hospital length of stay.

At the time of discharge from hospital, 93% of patients had no documented complication. In-hospital mortality was recorded at just 0.1%, showing an extremely low death rate associated with THA, and the most common cause of postoperative death was a cardiac-related event. The GLORY in-hospital mortality rate was less than that reported in the Norwegian Arthroplasty Registry, for which postoperative mortality at day 20 was 0.4%, at day 60 was 0.8% and at day 90 was 0.9%, with most deaths being attributed to vascular causes.[33] A full account of the complications and functional outcomes following THA and TKA in GLORY is given in this supplement in the article by Cushner and colleagues.[10]

Total Knee Arthroplasty

Demographic Data on Total Knee Arthroplasty. As shown in Table VI, data were collected on 8,325 patients undergoing TKA at 96 of the 100 hospitals from the 13 countries participating in GLORY. The median age of patients undergoing TKA was 69 years in the United States and 71 years in other participating countries. As with THA, a higher percentage of women underwent TKA than men in both the United States (62%) and other countries (72%). Patients had a median BMI of 31 kg/m^2 in the United States and 29 kg/m^2 in other countries, and again, the proportion of patients with a BMI > 30 kg/m^2 was higher in the United States (56%) than in other countries (42%). Health problems of severe or worse severity (ASA Grades III and above) were noted among 37% of US patients and 24% of patients from other countries. There was a 95% rate of osteoarthritis in the United States and 91% rate in other countries, with a 2% (United States) and 5% (other countries) incidence of rheumatoid arthritis and an overall 0.5% rate of osteonecrosis among TKA patients.

Table VIII. Blood Management in Total Knee Arthroplasty

	Countries		
	All	USA	Others
Median duration of tourniquet use, min (IQR)	71 (60–90)	69 (57–85)	75 (60–90)
Preoperative autologous blood management, %	21	27	13
Blood salvage, n	5,221	2,765	2,456
Total, %	31	41	19
Intraoperative, %	0.7	0.7	0.7
Postoperative, %	19	25	13
Both, %	11	16	6
Blood transfusion*, n	6,073	3,073	3,000
Total, %	42	38	46
Autologous, %	24	28	20
Donor, %	20	12	29

*Patients could receive more than 1 type of transfusion.

Table IX. Total Knee Arthroplasty Implant Selection*

	Countries		
Implant	All	USA	Others
Patients, n	8,325	5,209	3,116
Prosthesis fixation			
Cemented	90	91	89
Porous	9	8	10
Hydroxyapatite	0.8	1	0.6
Other	0.1	0.1	0.1
Tibial component			
Cemented	95	95	94
Porous	5	4	6
Hydroxyapatite	0.3	0.2	0.5
Other	0.1	0.1	0
Patellar component			
Not resurfaced	28	7	63
Cemented	70	91	36
Cementless	1	2	1
Prosthetic type			
Retained	45	44	46
Substitute	49	54	41
Constrained PCL	5	2	11
Meniscal bearing	3	1	5
Rotating hinge	1	0.4	3
Tibial component material			
All polyethylene	10	6	16
Metal-backed	85	94	70
Cross-linked polyethylene	30	15	55
Ceramic	0.01	0.02	0
Tibial polyethylene thickness > 8 mm	14	12	16
Patellar component material			
All polyethylene	81	89	50
Metal backed	9	9	12
Cross-linked polyethylene	19	9	57
Ceramic	0.07	0.04	0.2

*Patients could have more than 1 type of prosthetic, tibial component, and patellar component.
Abbreviations: PCL, posterior cruciate ligament.

Nineteen percent of US patients and 21% of patients from other countries had a prior contralateral TKA. Over half of US patients (52%) and patients from other countries (58%) had significant arthritic problems in other joints that could be expected to influence the outcome of their TKA. In particular, among US patients, 32% had contralateral knee arthritis, 3% had ipsilateral hip arthritis, and 3% had contralateral hip arthritis. In the entire GLORY cohort, 70% of patients had no history of previous surgery on the index joint. The most frequent forms of prior intervention were arthroscopy (10%), open meniscectomy (7%), and ligament reconstruction (1%). However, rates varied greatly according to country, with 96% of patients from the Australian center having a history of prior procedures to the knee, but only 9% of patients from the Japanese center having undergone prior knee surgery before the index TKA. It was noted that 62% of patients had a documented varus deformity, 20% had a valgus deformity, and 18% had neutral or insignificant varus/valgus alignment prior to surgery.

In GLORY, TKA patients were more likely to be women, were of age 65 to 75 years, typically had a history of osteoarthritis, and tended not to have undergone previous orthopedic surgery. These basic demographic findings reflect the reports of other orthopedic registries and large-scale studies in orthopedic patients.[15,34]

Procedure Used for Total Knee Arthroplasty. The anteromedial approach was most commonly taken for TKA procedures in the GLORY population, being used in 88% of cases (Table VII). By contrast, just 6% of surgery was performed through a subvastus approach; most of these procedures were in the United States (7% were performed using a subvastus approach) and in the center in Germany (18% were performed using a subvastus approach). On balance, a subvastus approach allowed quicker surgery (93% of subvastus surgery was performed within 2 hours) than anteromedial and anterolateral approaches (86% and 80% of these cases were complete within 2 hours; $P<.01$ for any rate difference). Length of surgery was found to have a significant association with the rate of fracture ($P = 0.03$). When surgery lasted ≥ 2 hours, the fracture rate was 0.9% compared with 0.2% for surgery lasting < 2 hours. This association was not found to be significant when data for the United States alone or for other participating countries alone were evaluated, and no other associations were found between length of surgery and any in-hospital or post-discharge complication.

With regards to anesthesic and analgesic practices for TKA, 43% of patients had general anesthesia, 46% received spinal anesthesia, and 20% had an epidural. Some patients had combination anesthesia (Table VII). A continuous epidural catheter for analgesia was used in 25% of patients.

Overall, 31% of patients were managed with blood salvage, and this generally occurred postoperatively (62% of salvage patients) (Table VIII). Blood salvage was most commonly used in the United States (41%) and in centers in the United Kingdom (45%) and Italy (44%). Preoperative blood transfusion (autologous; median volume of 395 mL) was used in 21% of TKA patients, and 42% of all patients received 1 or more unit of blood after surgery.

Table X. Length of Hospital Stay and Discharge Disposition After Total Knee Arthroplasty

Country	Patients, n	Median Length of Hospital Stay, Days (IQR)	Discharge, %	
			Home	Rehab. Center /Other
All	8,325	4 (3–9)	58	42
Australia	238	6 (5–7)	73	27
Brazil	26	7 (6–7)	96	4
Bulgaria	6	21 (20–25)	100	0
Canada	342	5 (4–6)	31	69
Colombia	111	4 (3–6)	99	1
Germany	615	12 (9–15)	69	31
Italy	864	10 (9–12)	71	28
Japan	22	21 (19–23)	100	0
Poland	327	16 (14–20)	93	7
Spain	229	11 (9–13)	99	0.4
Turkey	127	12 (10–15)	98	2
UK	209	9 (8–10)	94	6
USA	5,209	3 (3–4)	48	52

Abbreviations: IQR, interquartile range

Use of VTE prophylaxis in TKA patients was high. In hospital, 99% of TKA patients were given some form of VTE prophylaxis, but only 36% of patients continued to receive prophylaxis after discharge (Table VII). A more comprehensive account of VTE-prophylaxis practices has been reported elsewhere.[9,17] In TKA patients, the regimen of antibiotic treatment for prophylaxis against infection was > 24 hours in 46% of patients, ≤ 24 hours in 44% of patients, and a single dose in 10% of patients (Table VII).

Tourniquet Use During Total Knee Arthroplasty. Use of an intraoperative tourniquet during TKA is widespread, although variations in frequency of use, duration of application, and timing of release have been reported in the literature. A tourniquet is thought to reduce blood loss by helping to maintain a bloodless field. Debate surrounds the issue of whether a tourniquet should be released during surgery and after cementing, or after completion of the entire surgical intervention.[35-37] In GLORY the median duration of tourniquet use was 71 minutes for the entire population (Table VIII), although geographic differences were evident, with patients in Italian GLORY centers having a tourniquet in place for a median of 60 minutes as compared with 95 minutes in Colombia.

Implant Selection in Total Knee Arthroplasty. In most countries participating in GLORY, 99% to 100% of TKA patients received a cemented prosthesis (Table IX). Geographic variation in practice was evident in the management of the patellar component. Whereas over 90% of patients in the United States had cemented patellar components, only 36% of patients in other participating countries had a cemented patellar component.

Most (85%) tibial components were metal-backed, while patellar components were all-polyethylene in 81% of cases. Median tibial polyethylene thickness was 1 mm; in 14% of cases the thickness was > 8 mm.

The GLORY population reveals a fairly even distribution of cruciate-retaining versus cruciate-sacrificing implants. In 45% of TKAs in GLORY, a posterior-cruciate-ligament-retaining prosthesis was used, whereas in 49% of cases, a substituting prosthesis was used. Only 3% of TKAs used a meniscal-bearing prosthesis and 1% a rotating hinge, with these cases most likely in patients with significant preoperative instability. As in THA, there is a wide and ever-increasing choice of devices available to surgeons performing TKA, yet a study conducted in the United Kingdom suggests that clinical evidence is often lacking to support implant choice. More than half (54%) of the implant devices available in the UK orthopedic market for TKA were found to have no peer-reviewed evidence to support their use; this highlights the difficulties surgeons face when deciding which implant is best suited to a patient's immediate and long-term orthopedic needs.[38]

Although cementless fixation is widely used in THA, it is used less commonly in TKA. Some studies suggest a good or similar outcome at 5 to 10 years for cementless TKA compared with a cemented prosthesis,[39,40] whereas others suggest higher loosening and revision rates with cementless fixation[41,42] and particularly with metal, tibial, and patellar components.[43,44] The age of the patient and physical activity may impact implant selection and also the choice of technique for fixation in TKA. Cementless TKA has been reported to be reliable in younger (< 50 years of age) and physically active patients.[45] In this group of patients, the use of mobile-bearing knees, which are thought to reduce wear, has been shown to yield good clinical results and high rates of prosthesis survival.[46-48]

Postoperative Management of Total Knee Arthroplasty Patients. GLORY patients undergoing TKA were discharged to their home after surgery in 58% of cases and to a rehabilitation or other facility in 42% of cases (Table X). The majority of patients (88%) received a form of physical therapy after discharge from the acute care setting. Geographic variations were apparent in the postoperative management of TKA patients. In participating centers in the United Kingdom, 94% of patients were discharged home (with a median hospital stay of 9 days), whereas in Colombia centers, 99% went home (median stay of 4 days). In the United States, 48% of patients were discharged home (median stay of 3 days), and in Canada, 31% of patients went home (median stay of 5 days).

As with THA, when patients could not be sent to rehabilitation facilities or offered post-acute rehabilitation at home, length of stay in hospital was longer. The median stay for patients discharged home was 5 days and for those sent to rehabilitation was 4 days. In-hospital mortality after TKA was 0.1%, showing an extremely low death rate associated with TKA, and the most common cause of death was a cardiac event. The majority of TKA patients (92%) were discharged without a documented complication (see also Cushner and colleagues[10]).

Differences Between Total Hip Arthroplasty and Total Knee Arthroplasty Practices

In many regards, the demographics and the management of THA and TKA patients run in parallel. However, GLORY shows that TKA patients are typically older than THA patients, have a higher BMI, and have a poorer health status (all $P < .001$). TKA patients were also more likely to undergo surgery taking less than 2 hours ($P<.001$), have had previous surgery on the same joint ($P< .001$), and have had prior contralateral surgery ($P =.0004$) than THA patients. During orthopedic procedures, more patients undergoing TKA, compared with patients undergoing THA, received continuous epidural analgesia ($P<.001$), and cementing of implants appeared to be more common in TKA than in THA.

Conclusions

This review of international orthopedic practice based on data from GLORY demonstrates many similarities in the type of patients and in the general intraoperative and postoperative approaches used to care for patients who have undergone THA and TKA. Many aspects of orthopedic practice differ from country to country. There is notable variation in the choice and selection of prostheses, fixation of implants, length of hospital stay, and discharge disposition. Although there were relatively few centers in some countries, the differences in practice highlighted by GLORY are important.

GLORY shows that, in most countries, THA surgery is performed through a posterior or anterior lateral approach, with surgery typically falling within 2 hours. Cementless fixation in THA is common. The practice for TKA is to perform prosthesis placement through an anteromedial approach, and GLORY suggests a predominance of cemented fixation. As with THA, surgery typically lasted under 2 hours. Functional outcomes are discussed by Cushner and colleagues.[10]

Although prophylaxis for heterotopic ossification is not widely practiced after THA, the use of antibiotics and VTE prophylaxis is standard in patients undergoing either THA or TKA. This latter observation may, however, be skewed by the voluntary nature of the registry and does not take into account the appropriateness of prophylaxis measures taken. Patients are typically discharged to home after their acute hospital stay, and there is a universal emphasis on providing post-discharge physical therapy following both THA and TKA.

GLORY provides a unique source of information on patient demographics and patterns and practices in THA and TKA orthopedic care. By documenting variations in choice of implant, nuances in surgical technique, and differences in preoperative, perioperative, and postoperative approaches to patient care, it may be possible to identify factors that have important effects on the clinical and functional outcome following major orthopedic surgery.

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Practice Patterns in the Use of Venous Thromboembolism Prophylaxis After Total Joint Arthroplasty—Insights From the Multinational Global Orthopaedic Registry (GLORY)

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Abstract

The Global Orthopaedic Registry (GLORY) offers insights into multinational practice patterns of venous thromboembolism (VTE) prophylaxis in orthopedic surgery, based on data from 15,020 patients undergoing primary total knee arthroplasty or primary total hip arthroplasty from 2001 to 2004.

Registry data show that the first choice for in-hospital VTE prophylaxis was low-molecular-weight heparin. Multimodal prophylaxis was common. Warfarin was more widely used in the United States than elsewhere in the world. GLORY data suggest that real-world practice often fails to meet the standards for prophylaxis recommended in the American College of Chest Physicians evidence-based guidelines, particularly in the United States. However, many US orthopedic surgeons may follow other practice guidelines, causing an underestimation of prophylaxis use in this study. Warfarin use in the United States often failed to achieve recommended target international normalized ratio (INR) values.

This paper reviews the GLORY practice findings in light of the contemporary literature on best practices for VTE prophylaxis in orthopedic patients.

Orthopedic surgery carries a high risk of venous thromboembolism (VTE). Without prophylaxis, between 41% and 85% of patients who undergo high-risk procedures such as total hip arthroplasty (THA) or total knee arthroplasty (TKA) could be expected to develop subclinical deep vein thrombosis (DVT) and up to 10% may develop the potentially life-threatening complication of symptomatic pulmonary embolism (PE).[1-4]

For a number of years, evidence-based guidelines have been available to guide clinical practice on the use of VTE prophylaxis.[1,2,5] Both the International Union of Angiology guidelines[5] and the American College of Chest Physicians (ACCP) guidelines[1,2] summarize the strong evidence base supporting the use of prophylactic drugs such as low-molecular-weight heparin (LMWH) and warfarin for the prevention of VTE associated with THA and TKA (Table I). Similarly, the American Academy of Orthopaedic Surgeons (AAOS) has released guidelines for the prevention of PE,[6] recommending prophylaxis with aspirin, LMWH, synthetic pentasaccharides, or warfarin for patients undergoing THA or TKA and at standard risk of both PE and major bleeding.

However, the translation of evidence-based guidelines into everyday clinical practice is not immediate. In elective orthopedic surgery, as in other fields of medicine, adoption of recommendations relies on a combination of factors. These include the widespread distribution of guidelines and educational initiatives to reinforce the medical issues highlighted in published recommendations, together with ongoing audit and feedback to clinicians and surgeons on the impact and benefits of adopting new protocols and practices.[7-10]

In this paper we examine the practice patterns of VTE prophylaxis as analyzed in the multinational Global Orthopaedic Registry (GLORY). GLORY offers insights into "real-world" practice in 100 hospitals across 13 countries, and it provides data on large numbers of consecutively enrolled patients who have undergone elective THA or TKA and who have been followed up for a post-surgery period of 3 and 12 months. The findings of GLORY highlight both major differences and minor nuances in the use of VTE prophylaxis in different geographical regions, allow an assessment of how well current ACCP-guideline recommendations are being adhered to, and provide a valuable benchmark against which to review the contemporary literature providing guidance on VTE prophylaxis in orthopedic surgery.

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Table I. Guideline Recommendations for the Prevention of Venous Thromboembolism According to the American College of Chest Physicians 2001 (Geerts[1])

Prophylaxis Method	THA	TKA
LMWH	Timing: started 12 h before surgery, 12 to 24 h after surgery, or 4 to 6 h after surgery at half dose and continuing full dose next day Duration: at least 7 to 10 days	
Warfarin	Timing: started preoperatively or immediately after surgery Duration: at least 7 to 10 days Target INR: 2.5; range, 2 to 3	
IPC	Not recommended	Optimal use is an alternative option

Abbreviations: INR, international normalized ratio; IPC, intermittent pneumatic compression; LMWH, low-molecular-weight heparin; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Methods

The methodology of data collection for GLORY is described in detail by Anderson.[11] In brief, the registry enrolled 15,020 patients from 100 hospitals in 13 countries (Australia, Brazil, Bulgaria, Canada, Colombia, Germany, Italy, Japan, Poland, Spain, Turkey, United Kingdom, United States) between June 2001 and December 2004. Patients eligible for enrollment in GLORY were those undergoing elective primary THA or TKA and for whom a 12-month clinical follow-up period was feasible. In GLORY, 70% of enrolled patients had completed follow-up at either 3 and/or 12 months.

Data on patient demographics, primary diagnosis, pre-existing comorbid conditions, length of hospital stay, type of anesthesia, VTE prophylaxis (including type and duration), in-hospital complications, discharge disposition, and patient self-reported quality of life were gathered using standard case report forms (CRFs). Analysis of in-hospital practices are based on the entire cohort of GLORY patients; however, analyses requiring duration of prophylaxis information are based on the 8,160 patients in GLORY with confirmed duration of prophylaxis as assessed by a completed follow-up form. As this data was only collected in version 2 of the CRF (from January 2002 onwards), these 8,160 patients with follow-up are taken from a population of 11,222 patients (73% follow-up rate). Chi-square or Fisher's exact test was used to test for rate differences in different groups. Wilcoxon's rank sum test or analysis of variance was used to test group differences between continuous variables.

Results

Use and Type of Prophylaxis Against Venous Thromboembolism

Data from GLORY showed that over 99% of patients undergoing THA or TKA received some form of VTE prophylaxis.[12] The rate of use of prophylaxis was 99.5% in patients undergoing THA and 99.2% in patients undergoing TKA.[12] Furthermore, 95.4% of patients received some form of ACCP 2001–recommended prophylaxis (93.2% of THA patients and 97.6% of TKA patients).[12]

The most frequently adopted forms of in-hospital VTE prophylaxis were LMWH (given to 67% and 63% of THA and TKA patients, respectively), elastic stockings (57% and 58%), intermittent pneumatic compression (IPC) devices (40% and 47%), and warfarin (30% and 31%).

Clinical Practice Variations

Analyses of VTE prophylaxis choice according to geographical region reveal variations in practice between the United States and the other participating countries (Figure 1). Practice in the United States appears to rely on a number of different methods of prophylaxis, with LMWH being one of several methods employed. Furthermore, most physicians in the United States use more than one modality (mechanical and pharmacological) in combination. Intermittent pneumatic compression was used for only a short period in-hospital (median, 4 days for both THA and TKA) and tended to be used almost exclusively in combination with pharmacological prophylaxis (90% and 87% for THA and TKA, respectively). In the other participating countries, LMWH appears to be the cornerstone of VTE prophylaxis and is complemented by the use of stockings, while warfarin and IPC are rarely used. Data from GLORY on post-discharge VTE prophylaxis

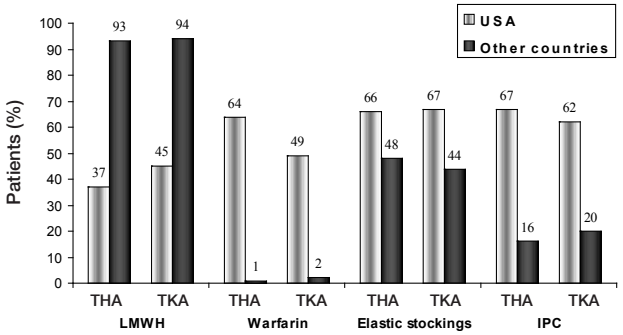

Figure 1. GLORY: Practice variation between the United States (USA) and the other participating countries for type of in-hospital VTE prophylaxis. Abbreviations: GLORY, Global Orthopaedic Registry; IPC, intermittent pneumatic compression; LMWH, low-molecular-weight heparin; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Table II. GLORY: Compliance With the 2001 American College of Chest Physicians Guidelines for Pharmacological Thromboprophylaxis Following Total Hip Arthroplasty or Total Knee Arthroplasty[12]

	THA		TKA	
	USA	Other Countries	USA	Other Countries
Full compliance with ACCP guidelines	47%	62%	61%	69%
LMWH				
Full compliance (timing and duration)	63%	67%	72%	73%
Timing	91%	80%	90%	85%
Duration	70%	85%	80%	85%
Warfarin				
Full compliance (timing, duration, target INR)	33%	N/A	48%	N/A
Timing	96%	N/A	98%	N/A
Duration	85%	N/A	74%	N/A
Target INR	36%	N/A	54%	N/A

Abbreviations: ACCP, American College of Chest Physicians; GLORY, Global Orthopaedic Registry; INR, international normalized ratio; LMWH, low-molecular-weight heparin; N/A, not applicable; THA, total hip arthroplasty; TKA, total knee arthroplasty; USA, United States.

revealed that regional differences persist once patients leave hospital (Figure 2).

Use of warfarin is particularly high in the United States compared with other participating countries (55% vs 1% of patients received in-hospital warfarin, respectively), a preference that has been reported previously.[13-15] Conversely, in the other countries represented in GLORY, LMWH is the anticoagulant of choice (93% and 42% of patients received in-hospital LMWH in the other countries and in the United States, respectively). Direct comparisons show that LMWH is at least as safe and efficacious as warfarin in THA,[16-18] and is as safe as, and more efficacious than, warfarin in TKA[19,20] or when compared across all orthopedic surgery.[21] Reasons for the widespread preference for LMWH among European orthopedic surgeons may

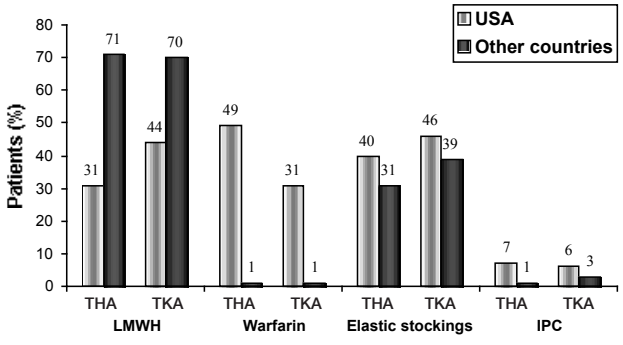

Figure 2. GLORY: Practice variation between the United States (USA) and the other participating countries for type of post-discharge VTE prophylaxis. Abbeviations: IPC, intermittent pneumatic compression; LMWH, low-molecular-weight heparin; THA, total hip arthroplasty; TKA, total knee arthroplasty.

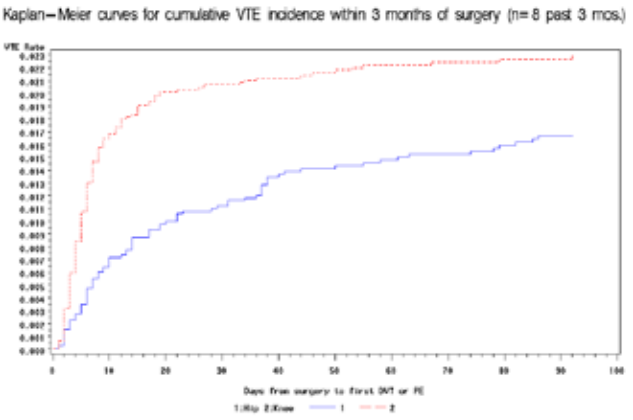

Figure 3. Kaplain-Meier curve for cumulative incidence of venous thromboembolism (VTE) events in total hip arthroplasty and total knee arthroplasty patients in GLORY. Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism.

include concerns about the less predictable pharmacological and clinical profile of warfarin compared with LMWH. In addition to its well-known interactions with several commonly used drugs and some foods,[22,23] warfarin is associated with a slow onset of antithrombotic activity (taking up to 60 hours to become effective),[24] displays a variable patient response that affects its therapeutic index,[25] and requires close assessment by frequent laboratory monitoring.[26]

The use of elastic stockings in nearly 60% of THA and TKA patients in GLORY is interesting. Although elastic stockings can be used without safety risks to the patients, there have been few studies investigating the safety and efficacy of elastic stockings as prophylaxis in orthopedic surgery patients. In a placebo-controlled study of LMWH for prevention of VTE following orthopedic surgery in which both groups wore elastic stockings, the rate of VTE was 59% in the elastic stockings–alone group.[27] This suggests that elastic stockings alone can not be considered to be suitable prophylaxis in this surgical setting.

Duration of Prophylaxis Against Venous Thromboembolism

Data from GLORY showed that for patients undergoing orthopedic surgery, median duration of in-hospital prophylaxis was 5 days. When warfarin was used (almost exclusively in the United States), prophylaxis was continued after discharge in 72% of patients, for a median total duration of 34 days (3 days in-hospital and 30 days post-discharge). Although the median duration of warfarin was similar for TKA and THA patients, a higher proportion of TKA patients received prophylaxis for a shorter duration compared with THA patients. When LMWH was the preferred choice for prophylaxis, it was generally given for a longer period to THA patients (median, 29 days worldwide) than to TKA patients (median, 14 days worldwide).

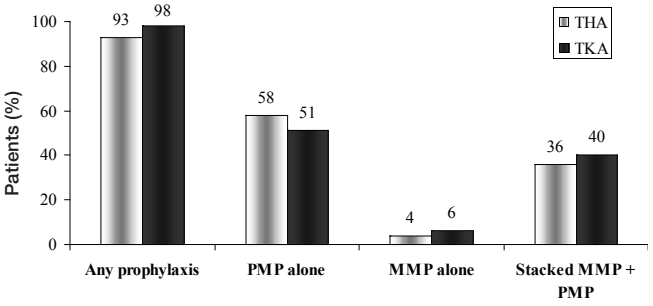

Figure 4. In-hospital Grade 1A recommended mechanical and pharmacological venous thromboembolism prophylaxis in THA/TKA patients. Patients received a grade 1A recommended prophylaxis type in-hospital according to Geerts and colleagues[2] (2004), but their care was not necessarily fully compliant with the guidelines regarding duration, dose, and timing. Abbreviations: MMP, mechanical methods of prophylaxis; PMP, pharmacological methods of prophylaxis; THA, total hip arthroplasty; TKA, total knee arthroplasty.

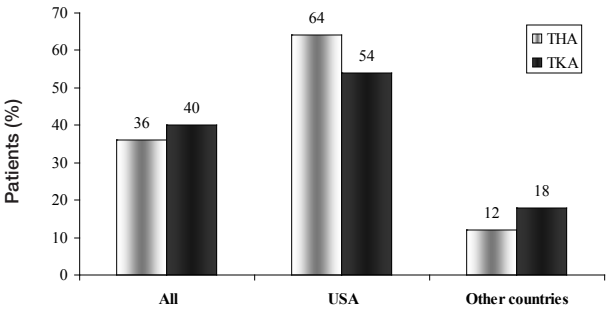

Figure 5. Concomitant mechanical and pharmacological venous thromboembolism prophylaxis in THA compared with TKA patients by region. Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty; USA, United States.

The differences in approach to duration of VTE prophylaxis following TKA and THA probably reflect an appreciation of the documented difference in time to a VTE event following these high-risk orthopedic procedures. In a large-scale community-based study, the median time to diagnosis of VTE following THA was 17 days after surgery, compared with 7 days after TKA ($P<.001$).[28] Furthermore, in placebo-controlled randomized trials, ongoing LMWH prophylaxis continued for 3 weeks after discharge effects a significant 65.5% relative risk reduction in VTE in THA patients compared with a shorter treatment duration ($P<.001$) and has less pronounced benefits in TKA patients.[2,4,29] Similar findings were observed in GLORY, as has been previously published (Figure 3).[30] In GLORY, prophylaxis with LMWH seemed to reflect the VTE time course difference between THA and TKA more strongly than prophylaxis with warfarin.

Stacked and Sequential Modalities for Prophylaxis Against Venous Thromboembolism

Although clinical studies of VTE prophylaxis typically evaluate a single method or "modality" of prophylaxis, in everyday practice, several forms of prophylaxis (pharmacological and mechanical) are often used concurrently or consecutively to provide what may be optimal protection against VTE risk. This is termed multimodal prophylaxis. Concurrent use of modalities is termed "stacked" prophylaxis, while consecutive use of modalities is referred to as "sequential" prophylaxis. There are few studies available evaluating the safety and efficacy of multimodal prophylaxis in randomized controlled clinical trials. Data from GLORY showed that multimodal prophylaxis is commonly used in major orthopedic surgery, especially in the United States (Figures 4, 5).

Some 99% of patients in GLORY received at least 1 modality in the hospital, 68% of patients received more than 1 modality, and 38% were given stacked mechanical and pharmacological modalities of prophylaxis. Assessment according to type of surgery revealed that 40% of TKA patients and 36% of THA patents received stacked modalities, with large differences again noted between the United States and the other participating countries. US surgeons were much more likely to stack modalities for TKA and THA (54% and 64% stacking, respectively) than surgeons in other countries (18% TKA and 12% THA stacking, respectively; $P<.001$ for both).

It can be speculated that US surgeons stack prophylactic modalities in order to maximize protection of their patients during the postoperative window prior to initiation of LMWH prophylaxis or while waiting for an appropriate INR to be achieved through use of warfarin prophylaxis. Further studies in the form of controlled trials are however required to investigate the clinical safety and efficacy of multiple types of prophylaxis in patients undergoing total joint arthoplasty.

GLORY and Compliance With Guidelines on Prophylaxis Against Venous Thromboembolism

As described earlier, 2001 guidelines on VTE prophylaxis following orthopedic surgery recommended the use of LMWH for patients undergoing TKA or THA, with prophylaxis started preoperatively or postoperatively and continued for at least 7 to 10 days or the use of warfarin started preoperatively or immediately after surgery and continued for 7 to 10 days[1] in order to achieve target INR in the range 2 to 3[5] (Table I). In the 2004 update of the ACCP guidelines, a minimum duration for prophylaxis of 10 days is indicated, with extension to 28 to 35 days recommended for total hip replacement.[2]

The GLORY data suggest that overall compliance with the 2001 ACCP recommendations was lower in the United States than in the other participating countries (Table II).[12] Full compliance with the ACCP recommendations on VTE prophylaxis in THA was just 47% in the United States compared with 62% in other countries, and while compliance was better in TKA management, the figure of 61% in the United States was still lower than the 69% rate achieved in other countries.

The literature suggests that in the management of general hospitalized medical and surgical patients, compliance with VTE prophylaxis guidelines varies greatly according to patient risk category, hospital, and country.[31-33] There is evidence that some physicians find it difficult to assess patient risk for VTE and often fail to choose appropriate prophylaxis even when a risk category is established.[31,32] One historical cohort study noted that failure to give prophylaxis was the most common reason for otherwise preventable VTE cases, while inadequate duration of prophylaxis was implicated in a further 23% of patients, and incorrect choice of prophylaxis in 20%.[33] However, it is important to note that risk stratification is more applicable to medical patients than to orthopedic surgery patients, as pharmacological prophylaxis is recommended in all orthopedic patients except for individuals with a contraindication.[2]

In total hip and knee arthroplasty, compliance with VTE prophylaxis guidelines has been reported to be good. A survey of 10 teaching and community-based hospitals in the United States published in 2000 found that the 1995 ACCP guidelines for use of grade A prophylaxis (prophylaxis recommendation based on consistent results of randomized clinical trials) were followed in 84.3% of THA cases and 75.9% of TKA cases.[7] A larger-scale registry study conducted in the United States during 1996 to 2001 that assessed data from over 9,000 THA patients and almost 14,000 TKA patients drawn from 319 hospitals (the Hip and Knee Registry) showed that compliance with ACCP recommendations for adequate VTE prophylaxis during in-hospital stay was 89% in THA patients and 91% in TKA patients; after hospital discharge, compliance was 67% in THA patients and 66% in TKA patients.[1,14] When interpreting such database findings, it is important to consider the definitions applied to describe compliance. Ahmad and colleagues[31] did not strictly define compliance with the guidelines, while the registry report of Anderson and colleagues[14] based compliance on use of grade A recommended therapies. Other practice reviews went further in specifying that compliance must involve correct modality selection and adequate dosing,[7,32] and one review also required compliance with guidelines on dosing, timing, and duration of prophylaxis.[33]

In GLORY, prophylaxis was considered to be compliant with the 2001 ACCP guidelines if it matched the type, dose, frequency of dosing, starting time, and duration of prophylaxis. Additionally, in the case of warfarin, an INR of 2 to 3 had to be reached (Table I).

Using these criteria, GLORY shows compliance rates for US practice that appear to be much lower than those previously reported.[7,14] This is probably not a reflection of a change in practice over time, but rather a stricter and more accurate view of compliance with all elements of the ACCP guidelines for VTE prophylaxis in THA and TKA patients. From the results described in this section, it would appear that the lack of compliance observed in the GLORY population is driven by physicians either not targeting an appropriate INR or failing to reach the target INR when using warfarin for VTE prophylaxis. It is also important to note that the GLORY registry was compared with the ACCP guidelines for the prevention of VTE.[1] However, the AAOS has also released guidelines for the prevention of PE following TKA and THA.[6] In this US-focused guideline, fondaparinux and aspirin are also recommended as appropriate prophylaxis. It is therefore likely that physicians who follow this guideline will be categorized as failing to meet guideline-recommendations in our study. While there continue to be discrepancies between the guidelines, it is likely that there will continue to be an overestimation of the number of physicians who appear to not follow guidelines.

Compliance With Guidelines on Warfarin Use

GLORY data show that warfarin is more widely used in the United States (administered to 55% of THA and TKA patients in hospital; Figure 1) than elsewhere in the world (< 2% of THA and TKA patients). Despite a preference for use of warfarin, our registry data reveal that compliance in the United States with ACCP recommendations for the use of warfarin was especially low, with only 33% compliance following THA and 48% compliance following TKA (Table II).

Current ACCP guidelines recommend a target INR for warfarin of 2 to 3,[2] yet in GLORY patients in the United States the target INR was set at 1.5 to 1.9 for 52% of THA patients and 33% of TKA patients. Although no conclusive clinical evidence currently exists for the efficacy of an INR of 1.5 to 1.9, it would be interesting to see a clinical trial investigate whether this approach, which has been adopted in many US sites based on physician experience, produces sufficient efficacy. In a study on DVT resolution, Caprini and colleagues[34] demonstrated that the degree of resolution was significantly linked to the INR values. Among warfarin-treated subjects, only 36% of THA patients and 54% of TKA patients actually achieved the guideline-recommended INR of 2 to 3, representing a large gap between the evidence-based guideline recommendations and real-world orthopedic practice. Among GLORY patients in the United States who were given warfarin and achieved the target INR, over half (64%) achieved the target at day 3 or later following surgery.

Under-anticoagulation (INR < 2) has been reported during warfarin prophylaxis in a number of clinical settings, with practice reviews highlighting a failure to achieve the target INR values required for adequate therapeutic responses.[23,35] Although VTE prophylaxis based on a low target INR of 1.5 to 1.9 has not been formally assessed in THA or TKA, it appears that achievement of target INR is likely to be important during the entire first 4 weeks following THA.[34] In this small-scale, open study assessing DVT incidence rates following THA in which warfarin prophylaxis was employed, patients who developed ultrasound-confirmed DVT had significantly ($P<.001$) lower INR values (< 2.0) during the second to fourth postoperative weeks.[34] This hypothesis-generating study suggests that there is a need to provide adequate prophylaxis throughout the entire period

during which patients are at risk. Furthermore, although early THA trials used a target prothrombin time of 14 to 16 seconds and thus a prothrombin ratio of 1.4 to 1.6,[36] this prothrombin ratio was not equivalent to the currently used INR measurement. In fact, a prothrombin ratio of 1.4 to 1.6 obtained using the strong laboratory thromboplastins then prevalent converts to an INR of 2.0 to 2.6.[37] Although it could be argued that ACCP evidence-based guidelines that explicitly recommend a target INR of 2.5 (range, 2.0-3.0),[2] may just reflect the current lack of clinical data regarding the safety and efficacy of a target INR < 2.0, there is extensive data from other clinical settings where an INR of 1.5 to 2.0 was less effective than an INR of 2.0 to 3.0.[38,39]

Compliance With Guidelines on Use of Low-Molecular-Weight Heparin

GLORY data showed that compliance with ACCP 2001 recommendations for the use of LMWH prophylaxis was higher than that for warfarin (Table II). Full compliance with dosing and duration of LMWH was observed in 70% of patients (73% TKA and 67% THA in other participating countries; 72% and 63%, respectively, in the United States) and lack of compliance was driven more by shortfalls in duration of prophylaxis than by timing of administration.

Improving Compliance With Guidelines

As can be seen from the results above, guideline compliance was low in GLORY patients for prophylaxis following THA and TKA. Even if the issue of the target INR for warfarin is removed from consideration, in which case both warfarin and LMWH would achieve approximately 70% ACCP-guideline compliance, 70% remains a value that requires further improvement, since all patients without a contraindication should be receiving pharmacological prophylaxis after orthopedic surgery.

A number of factors may contribute to the underuse of guidelines in real-world practice. As discussed previously, one potential reason is that physicians are following alternative guidelines to the ones studied here—for example, the AAOS guidelines on prevention of PE following TKA and THA.[6] Furthermore, according to a recent review, many physicians and surgeons continue to be unaware of the published guidelines on VTE prophylaxis.[40] Many surgeons continue to fear bleeding risks when using anticoagulant or antithrombotic drugs, and others consider the guidelines to be difficult to apply in everyday practice.[40] A meta-analysis of trials comparing warfarin with LMWH in THA patients has shown that the major bleeding rates are similar between these 2 treatments, with a slight excess of minor wound bleeding with LMWH.[41] In TKA patients, total bleeding rates were not significantly different between patients receiving warfarin and LMWH.[19] Furthermore, in a placebo-controlled study of LMWH in THA patients wearing elastic stockings, there was a similar rate of major bleeding in the 2 groups (2.5% and 2.4% in LMWH and placebo groups, respectively)[27] A recent meta-analysis of 11,485 combined THA and TKA patients found no significant difference in total bleeding rates between warfarin and LMWH (Relative Risk, 0.78 [95% CI 0.49-1.26]).[21]

Ahmad and colleagues[31] advocate better medical education to emphasize and improve the understanding of DVT risk stratification and heighten knowledge of recommendations for VTE prophylaxis and their benefits. Clinical support systems such as those used in a French orthopedic surgery department, where computer-based systems help to assess patient risk, direct prophylactic choice in line with current guidelines, and remind physicians and surgeons of deviations in prophylactic management, have been found to increase compliance with VTE guidelines from 82.8% to 94.9%.[42] Computer alert systems in the United States have also been shown to have a significant impact on VTE prophylaxis, almost doubling the use of pharmacological prophylaxis and reducing the risk of DVT and PE by 41% among high-risk hospitalized patients.[43]

It should be noted, however, that GLORY is a voluntary registry, and as such, it is likely that many of the surgeons who agreed to provide registry data already pay special attention to VTE prophylaxis and may therefore be providing higher levels of prophylaxis than surgeons in a random "real-world" hospital. This may therefore result in an overestimation of global practices in VTE prophylaxis use following THA and TKA in the GLORY registry. Furthermore, comparing the GLORY registry of 100 hospitals in 13 countries with a US-specific survey of American Association of Hip and Knee Surgeons (AAHKS) members[13] demonstrates discrepancies in the use of different pharmacological prophylaxis options. For example, in the US sites of the GLORY registry, 37% of THA patients and 45% of TKA patients received in-hospital LMWH. However, in the AAHKS survey, only 15.4% of THA patients and 18.0% of TKA patients received LMWH prophylaxis. Furthermore, 15.8% of THA patients and 18.4% of TKA patients received aspirin prophylaxis, a type of prophylaxis that was not often used in GLORY. It is therefore important to note that it may not be possible to generalize from the specific US hospitals in the GLORY database to the whole country.

Furthermore, it was compliance with the 2001 ACCP guidelines that was evaluated; the 2004 update, which recommends an increased duration of prophylaxis after THA,[2] became available only toward the end of the study period.

Screening for Deep Vein Thrombosis

The current ACCP guidelines give a grade 1A recommendation against routine screening for subclinical DVT before discharge from hospital.[2] This is based on large-scale trials that found routine screening to not be effective in the prevention of adverse clinical outcomes, or cost-effective.[44-47] Data from GLORY showed that 13% of THA and TKA patients underwent routine screening for DVT, with this practice more common in the United States (18%) than in the other participating countries (7%).

Conclusions

The registry data show that most orthopedic surgeons are committed to VTE prevention, with 99% using some form of prophylaxis during hip or knee replacement. Multimodal

prophylaxis is common, with widespread use of both pharmacological drugs and mechanical devices. However, the registry highlights that real-world practice often fails to meet the standards for prophylaxis as prescribed in evidence-based guidelines. Strict compliance with recommended prophylaxis was lower in the United States than in the other participating countries, although this may be due to the presence of alternative guidelines for these surgeons. This failure to comply appears to be due in part to a continued preference in the United States for warfarin as prophylaxis, despite difficulties with achieving adequate INR values while using warfarin. In the other participating countries, LMWHs are the favored method of VTE prophylaxis, and registry data suggest that compliance with recommended regimens is better with these drugs than with warfarin. As noted above however, it is likely that GLORY surgeons, although selected from a variety of geographical locations and hospital environments, are likely interested in quality improvement and thromboprophylaxis. This in turn is likely to impact the results, perhaps leading to a higher rate of interest in thromboprophylaxis than would normally be observed. In a recent US study, 8% of THA and TKA patients received aspirin alone for prophylaxis and 3% received no prophylaxis at all.[15]

As more prospective data become available in the form of randomized controlled trials and registries, a corresponding shift to evidence-based medicine is needed. The gaps between recommended and real-world VTE prophylaxis practices have been recognized throughout the expanding literature in this field. New initiatives involving better continuing education of physicians, novel computer-based support and alert systems, and the continued appraisal of practice through databases and registries such as GLORY will continue to drive improvements in care that will ensure optimal VTE prophylaxis for high-risk patients such as those undergoing major orthopedic surgery.[9,13,40,42,43] Although thromboprophylaxis should be systematic in surgical orthopedic patients, from the data presented in this paper, it seems clear that there is also an urgent need for education to improve the quality of prophylaxis, to ensure it is compliant with contemporary evidence-based medicine guidelines, in patients undergoing primary THA and TKA. It would also be interesting to re-analyze data from GLORY for compliance with other guidelines, such as the AAOS guideline for prevention of PE.

A great advantage of registries such as GLORY is their potential to gather information about the prevalence of real-life clinical practices that have not been validated. The frequent use of a low-target INR for warfarin prophylaxis after joint arthroplasty, and of stacked preventive modalities, indicates an urgent need for their formal evaluation through prospective clinical trials.

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Complications and Functional Outcomes After Total Hip Arthroplasty and Total Knee Arthroplasty: Results From the Global Orthopaedic Registry (GLORY)

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Abstract

The Global Orthopaedic Registry (GLORY) has been designed to monitor a broad range of complications and outcomes that occur following total hip arthroplasty (THA) and total knee arthroplasty (TKA). GLORY provides global "real-world" data, in contrast to the data generated by the controlled conditions of clinical trials.

The results to date show an overall incidence of both in-hospital and post-discharge complications of approximately 7% in THA patients and 8% in TKA patients. The most common in-hospital complications in THA patients are fractures (0.6%) and deep vein thrombosis (DVT) (0.6%), whereas in TKA patients DVT (1.4%) and cardiac events (0.8%) are most common. The most common post-discharge complications in both THA and TKA patients are reoperation due to bleeding, wound necrosis, wound infection, or other causes; and DVT. Bleeding complications were less common than other adverse events in both groups (in-hospital rates of 0.48% and 0.83%, respectively). Functional outcomes improved after surgery in both groups, as expected. Younger patients and patients who had been discharged directly to their homes seemed to have the greatest improvement in functional outcome after surgery.

The Global Orthopaedic Registry (GLORY) has been designed not only to monitor practices in orthopedic surgery but also to provide insights into complications and functional outcomes resulting from such surgery.

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Data on outcomes after total hip arthroplasty (THA) or total knee arthroplasty (TKA) have been collected from clinical trials that assess individual devices or from country-specific registries. The first registries to be established were the Swedish THA and TKA registries.[1,2] These, together with subsequent country-specific registries worldwide, have provided important information on the long-term outcomes following THA and TKA. Most registries focus on outcomes resulting from different types of implant and the factors that affect implant survival. As a result, they provide a valuable quality-improvement tool to identify inferior implants as early as possible,[1,3] but they offer relatively little information about other complications and functional outcomes.

GLORY has been designed to monitor a broader range of complications and outcomes than those related solely to implant survival.[4] As an international registry, it includes global, rather than country-specific or implant-specific, data. Data from GLORY can thus provide important insights into THA and TKA practices worldwide and also the incidence of different types of complications. Because of the worldwide nature of GLORY, some practice patterns, such as the relatively high prescription rate of low-molecular-weight heparin and the low rate of aspirin use for prophylaxis of venous thromboembolism (VTE) may not be representative of a US-specific population.

This paper reviews the incidence and nature of complications following THA or TKA as recorded in GLORY and compares these findings with those of previous studies.

Methods

GLORY is a multinational, observational study that has been designed to examine treatment practices in patients undergoing major joint replacement surgery. The methodology has been described in full by Anderson and colleagues.[5] The study was designed and is coordinated by the Center of Outcomes Research at the University of Massachusetts, USA, under the guidance of a Scientific Advisory Board. Full details of GLORY are available on the registry web site.[4]

A total of 156 surgeons have enrolled patients from 100 university-affiliated or community hospitals in 13 countries worldwide. Participating surgeons enrolled 15,020 patients who had undergone elective primary THA (6,695

Table I. Incidence of Complications Occurring in Hospital and After Discharge in GLORY

Complication	In-Hospital Complications		Additional Complications 3 Months Post-Surgery	
	THA (n = 6,695)	TKA (n = 8,325)	THA (n = 4,940)	TKA (n = 5,550)
One or more complications	486 (7.3%)	671(8.1%)	332 (6.7%)	445 (8.0%)
Fracture	41 (0.6%)	8 (0.1%)	19 (0.4%)	10 (0.2%)
Deep vein thrombosis	40 (0.6%)	113 (1.4%)	49 (1.0%)	38 (0.7%)
Dislocation	34 (0.5%)	3 (0.1%)	39 (0.8%)	3 (0.1%)
Nerve palsy	33 (0.5%)	14 (0.2%)	19 (0.4%)	11 (0.2%)
Wound infection	29 (0.4%)	35 (0.4%)	43 (0.9%)	94 (1.7%)
Reoperation	27 (0.4%)	42 (0.5%)	56 (1.1%)	126 (2.3%)
Bleeding—delayed discharge/ Major bleeding*	21 (0.3%)	26 (0.3%)	4 (0.1%)	8 (0.1%)
Cardiac events	29 (0.4%)	50 (0.8%)	10 (0.2%)	18 (0.3%)
Pneumonia	14 (0.2%)	29 (0.5%)	ND	ND
Pulmonary embolism	7 (0.1%)	23 (0.3%)	6 (0.1%)	6 (0.1%)
Death	9 (0.1%)	16 (0.2%)	16 (0.3%)	7 (0.1%)
Other**	236 (3.5%)	325 (3.9%)	149 (3.0%)	263 (4.7%)

* Bleeding defined as "Bleeding-delayed discharge" for in-hospital complications and defined as "Major bleeding" for additional complications 3 months post-surgery
** Unspecified.
Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty; ND, no data.

Table II. Incidence of Bleeding in Hospital and 3 Months After Surgery

Bleeding Type	In-Hospital Bleeding		Additional Bleeding 3 Months Post-Surgery	
	THA (n = 6,695)	TKA (n = 8,325)	THA (n = 4,940)	TKA (n = 5,550)
Bleeding necessitating reoperation	2 (0.03%)	9 (0.11%)	1 (0.02%)	3 (0.06%)
Bleeding-delayed discharge	21 (0.31%)	26 (0.31%)	0	0
Hematoma requiring evacuation	7 (0.10%)	25 (0.30%)	1 (0.02%)	4 (0.07%)
Epidural hematoma	1 (0.01%)	1 (0.01%)	0	0
Gastrointestinal bleeding	3 (0.06%)	15 (0.25%)	0	0
Other bleeding during surgery	2 (0.04%)	0	0	0
Major bleeding	0	0	4 (0.08%)	8 (0.14%)
Readmission due to bleeding	0	0	2 (0.04%)	1 (0.02%)
Any	32 (0.48%)*	69 (0.83%)*	8 (0.16%)	16 (0.29%)

* Significantly different, $P = .01$
Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty.

patients) or TKA (8,325 patients) between June 2001 and December 2004; revision procedures were excluded. In-hospital data were collected for all patients, and 70% of patients were followed up after 3 months and/or 12 months to collect data on post-discharge outcomes.

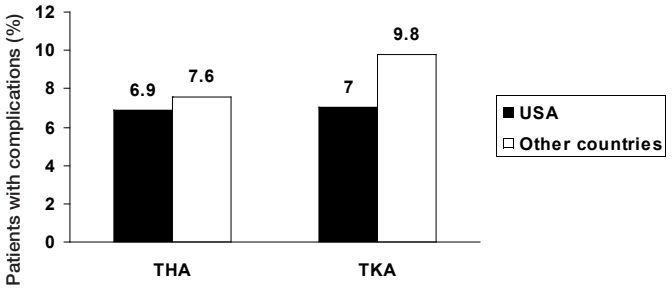
Participating surgeons or trained study coordinators collected data using standard case report forms, which were sent to the scientific coordinating center for entry into the database and for subsequent analysis. Data quality control was monitored using standardized query logic. Out-of-range or illogical responses were queried on a quarterly basis, and corrections were faxed to the scientific coordinating center.

Approval of the study was obtained from local ethics committees or institutional review boards, as required. When required by the Ethics Review Committee at each hospital, signed informed consent was obtained from patients prior to their enrollment. Chi-square or Fisher's exact test was used to test for rate differences in different groups. Wilcoxon's ranked sum test or analysis of variance was used to test group differences between continuous variables.

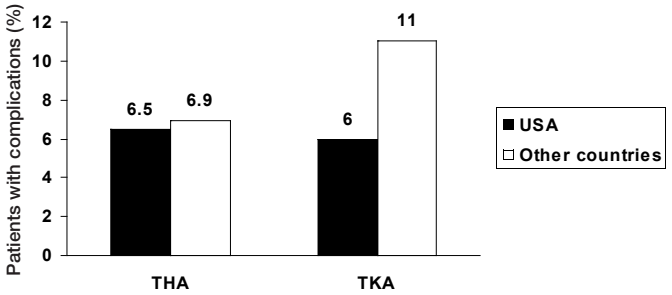
General Complications

Previous studies have identified a broad range of complications following THA[6,7] or TKA.[8] These include delayed wound healing or wound dehiscence; renal and urinary complications; cardiovascular complications, VTE including deep vein thrombosis (DVT) and pulmonary embolism (PE), myocardial infarction, or bleeding; and pneumonia and other respiratory complications.

The data from GLORY show a similar spectrum of complications (Table I). The overall incidence of both in-hospital and post-discharge complications was approximately 7% in THA patients and 8% in TKA patients. However, the nature of the recorded complications was similar in all countries and all types of hospitals. The incidence of in-hospital and post-discharge complications was similar in the United States and in the other participating countries in THA patients ($P = .32$ and .60 for in-hospital and post-discharge, respectively), but was slightly higher in other participating countries than in the United States in TKA patients ($P<.001$ for both in-hospital and post-discharge; Figure).



a. In-hospital



b. Post-discharge

Figure. Incidence of in-hospital and post-discharge complications following total hip arthroplasty and total knee arthroplasty in the United States (USA) and the other participating countries. Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty.

In THA patients, the most common in-hospital complications were fractures and DVT, both of which occurred in 0.6% of patients, whereas in TKA patients the most common in-hospital complications were DVT (1.4%) and cardiac events (0.8%). The most common post-discharge complications in both THA and TKA patients were reoperation due to bleeding, wound necrosis, wound infection, or other causes (1.1% and 2.3%, respectively), wound infections (0.9% and 1.7%, respectively), and DVT (1.0% and 0.7%, respectively). Some complications, such as myocardial infarction and pneumonia, were uncommon in both groups, reflecting the fact that THA and TKA are elective procedures that are mainly performed in healthy patients.

The relatively low incidence of reoperations reported in GLORY is of interest, given the higher incidence reported in the Swedish hip and knee registries. As noted earlier, these focus largely on implant survival as a major outcome and document the reasons for reoperation or revision.[1] Of 229,031 primary THAs that were performed between 1979 and 2003, reoperation was necessary in 26,111 (11.4%).[2] The most common reason for reoperation was aseptic loosening, which accounted for 60.6% of reoperations, followed by dislocation (10.7%), deep infection (8.3%), and fracture (6.8%).[2] Among patients undergoing knee arthroplasty (both TKA and unicompartmental arthroplasty), a total of 1,902 of 41,223 (4.6%) primary arthroplasties that were performed between 1988 and 1997 had been revised by the end of this period.[8] The principal reason for revision (including revisions of arthroplasties that were performed before 1988) was loosening, which accounted for 44% of procedures. Approximately 50% of revisions were performed within 4 years of the primary arthroplasty; in particular, revisions due to infection or patellar problems were more common during the first 45 months than they were after the first 45 months.[9]

The higher incidence of reoperations seen in the Swedish registry data, compared with the GLORY data, may reflect the shorter follow-up period in GLORY and the fact that since the time the Swedish registry was started (as early as 1979) practice has improved with type of implants, antibiotics, and so on. It is difficult to compare the rates of other complications in the Swedish and GLORY registries because GLORY reports all complications, whereas the Swedish registries report only those that lead to reoperation. For example, DVT and cardiac events are relatively frequent complications in GLORY (Table I), whereas these tend to be unreported in the Swedish registries as they would not lead to revision.

A further registry-based study, which was conducted in Iceland, has reported markedly higher rates of dislocations (5%) and cardiac or cerebrovascular complications (3.1%) among THA patients than those reported in GLORY (Table I).[10] The incidence of wound infections (0.5%) and VTE, including both DVT and PE (1.5%), in this study were comparable with those in GLORY. However, as with the Swedish registries, these data are country-specific and, moreover, relate to a smaller patient population (548), who received a single type of implant.

Bleeding

Comparisons of bleeding rates in studies of THA and TKA patients are complicated because the definitions of clinically important or major bleeding have varied considerably between trials.[11] In GLORY, clinically important bleeding has been defined as "bleeding that is recorded by the surgeon as being outside the range of 'typical expected levels' of bleeding following THA/TKA, or bleeding that is cited as the cause of prolonged hospital stay." Clinically important bleeding included multiple types of bleeding (Table II), amongst others bleeding necessitating reoperation, bleeding-delayed discharge, and gastrointestinal bleeding. The incidence of such bleeding in GLORY was relatively

Table III. Incidence of Bleeding (Major or Minor) in Relation to Use of Thromboprophylaxis

	n (In-Hospital) / *n* (In-Hospital or 3 Month Post-Surgery Bleeding)	In-Hospital Bleeding	In-Hospital or 3 Month Post-Surgery Bleeding
LMWH alone	9,241/5,858	65 (0.7%)*	45 (0.8%)
Warfarin alone	4,148/1,431	14 (0.3%)*	9 (0.6%)
Both	485/308	8 (1.7%)	6 (2.0%)
Neither	1,146/563	14 (1.2%)	10 (1.8%)

* Significantly different, $P = .01$

Abbreviations: LMWH, low-molecular-weight heparin.

Table IV. Incidence of Venous Thromboembolism (DVT and PE) According to Patient Sex and Age

	DVT		PE	
	THA	TKA	THA	TKA
Total	1.6%	2.3%	0.24%	0.29%
Men	1.4%	1.6%	0.25%	0.32%
Women	1.7%	2.6%	0.25%	0.28%
Age < 65 years	1.4%	2.3%	0.23%	0.47%
Age ≥ 65 years	1.8%	2.2%	0.25%	0.21%

Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Table V. In-Hospital and Post-Discharge Mortality

	THA (n = 6,695)	TKA (n = 8,325)
Deaths in hospital	9 (0.1%)	16 (0.2%)
Deaths attributed to PE in hospital	0	2
Post-discharge deaths within 3 months of surgery*	16 (0.3%)	7 (0.1%)
Deaths attributed to PE post-discharge	1	0

* Median follow-up 3 months, range 1-18 months. Four additional TKA deaths occurred at 6-15 months post-surgery.
Abbreviations: PE, pulmonary embolism; THA, total hip arthroplasty; TKA, total knee arthroplasty.

low, both in THA patients (0.48% in hospital; 0.16% 3 months after surgery) and in TKA patients (0.83% and 0.29%, respectively; Table II). Some patients had both in-hospital bleeding and additional bleeding in the 3 months after surgery, so that overall, 29 of 4,940 THA patients (0.59%) experienced clinically important bleeding, compared with 59 of 5,550 (1.06%) TKA patients. Clinically important in-hospital bleeding, albeit rare, was significantly more common after TKA than after THA (0.83% vs 0.48%, respectively; $P = .01$, Table II). With this level of clinically important bleeding in GLORY, it was not possible to determine which factors were associated with an increased risk for bleeding. Blood transfusions were given to 57% of THA and 42% of TKA patients at a median volume of 600 mL (see also Waddell and colleagues[12] in this supplement for details on blood usage).

The results from GLORY are consistent with those of a recent systematic review,[13] which included data from 71 trials, involving 32,433 patients. This review compared different thromboprophylactic regimens in patients undergoing major orthopedic surgery (THA, TKA, or hip-fracture surgery). Major bleeding occurred in 632 patients (1.95%) receiving thromboprophylaxis, of whom only 118 (0.4%) required surgical or medical intervention; only 5 cases of fatal bleeding were identified. The most common location of bleeding was the wound site, which accounted for 71% of major bleeding episodes; 7% of episodes occurred in the gastrointestinal tract, and the remainder at other sites.[13]

Impact of Thromboprophylaxis on Bleeding Risk

Major or minor bleeding can occur in a significant proportion of patients who are undergoing major orthopedic surgery, even in the absence of thromboprophylaxis. For example, in a meta-analysis of 52 trials of thromboprophylaxis, involving almost 11,000 THA patients, the total incidence of minor and major bleeding in placebo-treated patients was 3.0% and 0.6%, respectively.[14]

The GLORY population consisted of a large sample of THA and TKA patients, of whom almost all (99% in both groups) received some form of thromboprophylaxis. Approximately two-thirds of patients in each group received low-molecular-weight heparin (LMWH) and approximately 30% in each group received warfarin. As shown in Table III, the incidence of bleeding, either in hospital or at 3 months after discharge, was low in these patients (0.8% in LMWH-treated patients; 0.6% in warfarin-treated patients). Data from randomized controlled trials and meta-analyses have shown that prophylactic doses of vitamin-K antagonists, low-dose unfractionated heparin (UFH), and LMWH are associated with little or no increase in the risk of clinically significant bleeding.[14,15] In the meta-analysis by Muntz and colleagues,[13] the relative risk of major bleeding with UFH, compared with LMWH, was 1.52 (95% CI, 1.04–2.23). In addition, fondaparinux, a synthetic pentasaccharide, was also associated with an increased risk of major bleeding, compared with LMWH (Relative Risk, 1.52; 95% CI, 1.11–2.09).

In GLORY, in-hospital bleeding was significantly less common in warfarin-treated patients than in those receiving LMWH (0.3% vs 0.7%, respectively; $P = .01$). This might reflect the delayed onset of the anticoagulant effect of warfarin, as a result of which the therapeutic effect might not have been achieved in many patients until after discharge from hospital. Furthermore, owing to the nature of the GLORY registry, physician perceptions regarding the risk of bleeding may have influenced the decision as to which drug to give the patient.

Vascular Complications

Venous Thromboembolism

The GLORY data reflect the incidence of VTE in a real-world setting, in contrast to those data that are generated in the rigorously controlled conditions of clinical trials. Thromboprophylactic practices vary widely between hospitals, and they are fully documented in the registry. As shown in Table I, DVT (confirmed by venogram or ultrasound) was one of the most common in-hospital and delayed complications in both THA and TKA patients enrolled in GLORY. The incidence of VTE (DVT and PE) in different patient subgroups is shown in Table IV. The overall incidence of DVT in-hospital and post-discharge was higher in TKA patients than in THA patients (2.3% vs 1.6%, respectively). In patients undergoing TKA, the incidence was higher in women than in men and was similar in older (age ≥ 65 years) and younger (age < 65 years) patients. In THA patients, the incidence of DVT was similar irrespective of sex or age. The incidence of

Table VI. Functional Outcomes After THA or TKA, Assessed by Means of the WOMAC and SF-8 Questionnaires, According to Patient Characteristics

	WOMAC				SF-8 Mental				SF-8 Physical			
	n	Pre	Post	Diff	*n*	Pre	Post	Diff	*n*	Pre	Post	Diff
THA	2662	42.7	76.6	33.9	2546	47.0	51.7	4.8	2546	31.4	43.8	12.4
TKA	2987	46.5	72.8	26.3	2802	48.8	51.1	2.2	2802	32.7	42.4	9.8
P value		<.0001	<.0001	<.0001		<.0001	.004	<.0001		<.0001	<.0001	<.0001
Male	2060	48.0	76.7	28.8	1939	50.0	52.6	2.7	1939	33.2	44.3	11.1
Female	3489	42.8	73.3	30.6	3311	46.7	50.6	3.9	3311	31.4	42.5	11.1
P value		<.0001	<.0001	.001		<.0001	<.0001	<.0001		<.0001	<.0001	.94
Age < 65 years	2156	43.2	74.5	31.4	2059	47.8	51.6	3.8	2059	31.7	43.5	11.8
Age ≥ 65 years	3459	45.7	74.6	28.9	3256	48.0	51.2	3.2	3256	32.3	42.8	10.5
P value		<.0001	.92	<.0001		.53	.07	.03		.01	.005	<.0001
Home	3251	45.2	75.6	30.4	3084	48.0	51.7	3.7	3084	32.5	44.1	11.6
Rehabilitation/ Other	2266	43.9	73.1	29.2	2141	47.9	50.9	3.1	2141	31.4	41.7	10.3
P value		.005	<.0001	.01		.79	.003	.03		<.0001	<.0001	<.0001

Abbreviations: Diff, difference in mean scores; Post, mean 3-months postoperative score; Pre, mean preoperative score; SF-8, SF-8 Health Survey; THA, total hip arthroplasty; TKA, total knee arthroplasty; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

PE was 0.2% to 0.3% in all subgroups except in men who underwent TKA and TKA patients under 65 years of age, in which the incidences of PE were slightly higher at 0.32% and 0.47%, respectively.

Similar findings were reported in a review of the epidemiology of VTE in patients undergoing major orthopedic surgery.[16] The data from 7 studies of pharmacologic or mechanical thromboprophylaxis in patients undergoing THA, TKA, or hip-fracture surgery suggest that the incidence of DVT is approximately 2.5% and that the risks of nonfatal or fatal PE occurring are approximately 1% and up to 0.4%, respectively.[16]

A further study has used data from the California Patient Discharge Series (a registry of discharge data from all nonfederal licensed hospitals in California) to investigate the incidence of symptomatic VTE in patients undergoing a variety of surgical procedures.[17] The incidence of VTE at 91 days in patients undergoing THA or TKA was 2.4% and 1.7%, respectively, of which 1.8% and 0.8% of cases, respectively, occurred after discharge. It should be noted, however, that information about the use of thromboprophylaxis was not available in this study.

A recent report has described the incidence of PE in 3,954 patients undergoing THA, TKA, or hip-fracture surgery, who were included in a prospective registry in Southern Norway between 1989 and 1998.[18] All patients received thromboprophylaxis with LMWH for about 10 days until discharge. A total of 50 cases (1.3%) of nonfatal PE were identified. Importantly, the incidence of PE remained elevated for at least 2 to 3 months after surgery in patients undergoing THA and for several weeks after surgery in TKA patients. This persistent risk, despite the use of thromboprophylaxis, has been attributed to the fact that risk factors for VTE may be present for longer than the normal period of thromboprophylaxis. Extended-duration thromboprophylaxis, which continued for up to 35 days after surgery, has been shown to reduce still further the risk of VTE after THA but not TKA.[19,20]

Mortality Associated With Venous Thromboembolism

Pulmonary embolism has been reported to account for approximately 10% of in-hospital deaths,[21,22] making VTE a major cause of mortality. Deaths that occurred either in hospital or post-discharge in the GLORY population are summarized in Table V. Overall, 25 of 6,695 (0.4%) THA patients and 23 of 8,325 (0.3%) TKA patients died in hospital or within 3 months after discharge, of whom 3 were believed to have died as a result of PE.

This low mortality rate is in marked contrast to data from the Norwegian Arthroplasty Register, which reported a 6% incidence of vascular death within 60 days after THA.[23] The mortality rate associated with PE or pulmonary infarction was 0.92%, and that associated with DVT was 0.28%. These higher rates, compared with the current GLORY results, may reflect improvements in surgical and prophylaxis techniques over the years.

Low rates of cardiac events occurred in the GLORY population, with 0.4% and 0.8% of THA and TKA patients, respectively, experiencing a cardiac complication.

Functional Outcomes

GLORY used a general health questionnaire, the SF-8 Health Survey (SF-8), and a disease-specific health questionnaire, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) to assess functional outcomes after THA and TKA. The SF-8 is an alternative form of the widely used SF-36 quality-of-life (QOL) questionnaire, which uses a single question to measure each of the 8 SF-36 domains (physical function, social function, role-emotional,

role-physical, bodily pain, general health, mental health, and vitality). The WOMAC is a self-administered questionnaire that assesses pain, stiffness, and physical function. Both the SF-36 and WOMAC have been shown to be valid tools to assess outcomes after THA.[24]

Table VI summarizes changes in SF-8 and WOMAC scores following THA or TKA in the GLORY population. Both measures showed, as expected, marked improvements after surgery. THA patients showed significantly lower scores before surgery than TKA patients, indicating that these patients experienced more pain and disability, and scores improved after surgery to a significantly ($P<.001$) greater extent in THA patients than in TKA patients. The WOMAC and SF-8 mental scores were significantly ($P<.0001$) lower in women than in men prior to and after surgery, although they improved to a significantly greater extent in women ($P = .0001$ for WOMAC; $P<.0001$ for SF-8 mental. Improvements in all scores after surgery were significantly lower in older patients (aged ≥ 65 years) than in younger patients, possibly reflecting the impact of comorbidity in older patients. Significantly greater improvements were also seen in patients who had been discharged to their homes rather than to rehabilitation facilities.

The WOMAC scores that were reported postoperatively are similar to those reported at 2 and 3 years after surgery in the Swedish National Total Hip Arthroplasty Register (a mean score of 74 at both time points).[25] This registry is also consistent with the GLORY data in that men showed higher postoperative QOL scores, as measured by the SF-36 questionnaire, than women.[26]

The finding in GLORY that patients ≥ 65 years showed poorer improvements in functional outcomes than younger patients is in contrast to a previous study in 454 patients undergoing THA or TKA.[27] In this study, there were no significant differences between the improvements in WOMAC and SF-36 scores after surgery in patients aged 55 to 79 years and in those aged ≥ 80 years. Similarly, the finding in the present study that patients who had been discharged to their homes had higher QOL scores than those who had been discharged to rehabilitation facilities is at variance with those of a previous study involving 96 total arthroplasty patients.[28] In the latter study, there were no significant differences in outcome scores between patients who had been discharged to a subacute rehabilitation program and those who had been discharged directly to their homes with physical therapy follow-up. These differences may reflect the impact of sample size: as a result of the large number of patients enrolled in GLORY, this study can more easily identify patient-related factors affecting functional outcomes.

Conclusions

Although a variety of complications have been reported to occur after THA or TKA, the GLORY data show that the incidence of major complications is low. The most common complications included reoperations, infections, DVT, and (in THA patients) dislocations. It is notable that clinically important bleeding was rare in the large sample of THA or TKA patients, essentially all of whom were given thromboprophylaxis.

The finding that DVT occurred in up to 1.4% of patients enrolled in GLORY shows that VTE remains an important potential complication of THA and TKA, despite the widespread use of thromboprophylaxis. This problem may be, at least partly, overcome by extending the duration of prophylaxis for up to 35 days after surgery, as has been shown to be effective in THA patients.[19,20]

The data from GLORY show that the functional outcomes after THA or TKA may depend on the patient's characteristics. Although total arthroplasty can markedly improve patients' functioning and general well-being, the greatest benefits seem to be achieved in younger patients and in patients who have been discharged directly to their homes.

In conclusion, GLORY provides contemporary data on outcomes that occur after THA or TKA; these data are derived from a global, real-world setting that clinical trials are unable to reproduce as the inclusion and exclusion criteria are limiting. GLORY has been able to recruit a large and diverse patient population, and hence it was able to identify factors affecting outcomes that may not be apparent in clinical trials. It is notable, however, that the physicians in GLORY prescribe aspirin for VTE prophylaxis less frequently than has been shown in other studies.[29]

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Lessons Learned From the Global Orthopaedic Registry (GLORY): Study Design, Current Practice Patterns, and Future Directions

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The previous articles in this supplement have recounted, in detail, a number of the findings of the Global Orthopaedic Registry (GLORY) and placed them within the context of current knowledge regarding anticoagulation in patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA). Furthermore, because of the multinational nature of GLORY, we have been able to provide a preliminary view of some of the geographical differences in orthopedic practices that occur.

The first article provided an introduction to GLORY's methodology, strengths, and limitations.[1] The 3 main papers in this supplement then showed GLORY results on orthopedic practice,[2] venous thromboembolism (VTE) prophylaxis practice after THA and TKA,[3] and complications and outcomes.[4]

The final GLORY data set encompassed 15,020 prospectively enrolled patients (6,695 THA and 8,325 TKA patients), with a 70% follow-up rate at 3 and/or 12 months. These patients were enrolled between 2001 and 2004, providing a contemporary data set assessing current clinical practice in THA and TKA. This data set will therefore provide a valuable reference source for current practice but should, of course, be superseded in the future.

The aim of the GLORY registry is to provide epidemiological data from real-life practice, supplementing information provided by clinical trials. These data can provide insight into possible disparities between evidence-based guidelines and real-life practice.[1] Furthermore, if sufficient data are collected, a risk factors assessment can be performed to identify risk factors for VTE, bleeding, or other complications.

It is widely accepted that a major role of registries is to provide data that are hypothesis forming and thus could require stricter evaluation in controlled clinical trials. A further advantage of this registry lies in its ability to help shape the future design of registries. To this end, we present here some of the more striking observations from GLORY, both in terms of conducting a registry of contemporary orthopedic procedures, and in suggesting some future work that has come out of the observations from GLORY.

"The aim of the GLORY registry is to provide epidemiological data from real-life practice, supplementing information provided by clinical trials."

Shaping Future Study Design

In an editorial relating to acute coronary syndrome registries, 12 key suggestions were defined to assess the quality of registries that, if followed, would improve the ability to compare between registries[5] (Table). Although these suggestions were made in relation to acute coronary syndrome registries, they are sufficiently broad to apply to other scientific areas. It is therefore interesting to note that the GLORY registry design met 11 of the 12 criteria defined in this editorial.

In order to produce a large volume of robust data, it is the opinion of the GLORY investigators that a designated central coordinating center is required. It has become clear that in order to run a large international registry and gather robust data, a central coordinating center and adequate funding are vital. Underestimating the required resources will likely lead to poor follow-up and, as a result, reduce the value of collected data. Furthermore, careful prospective design of the study (i.e., case report form [CRF] design) is important to ensure that valuable data are gath-

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Table. GLORY Compliance With Key Suggestions for Good Registry Design (made by Alpert JS. *Eur Heart J.* 2000;21(17):1399-1401)

Design Area	Key Suggestion	Present in GLORY Design?
Study design	Standardized disease definitions	√
	Standardized sampling techniques	√
Data collection	Randomized selection of hospitals/clinics or community-wide collection	x
	Clear understanding provided to participants on information required	√
	Reporting of all collected data	√
	Centralization of all data and analysis	√
	Professional statistician monitoring all data collection and analysis	√
	Accuracy and completeness of individual data sheets should be examined by central center	√
	IRB review and approval of registry protocol at each participating site	√
	Report the names of all participating investigators	√
	Sponsorship of the registry should be disclosed on all reports	√
	A PI or steering committee should maintain overall control of all facets of the registry's running	√

Abbreviations: IRB, institutional review board; PI, principal investigator.

ered without putting too much of a burden on study coordinators. If the time required to complete and submit the CRF is too lengthy, there will likely be an impact on enrollment and follow-up figures. It is therefore our recommendation that the initial step in setting up a new registry should be the formation of a steering committee whose members meet to discuss study design.

Current Practice Patterns

The data that have been outlined in the preceding pages of this supplement can be used in multiple ways. Firstly, they should be viewed as giving a contemporary view of current THA and TKA practices, from both the surgical and thromboprophylactic viewpoints, in both the United States and other countries. Secondly, they also provide valid epidemiological data on the rates of all complications in patients who underwent THA and TKA and received some form of prophylaxis. Thirdly, the data derived from this registry can be used to provide individual participating hospitals with specific feedback on practices as well as healthcare management with guidance on where improvement may be likely to be achievable. The provision of data back to participating physicians is valuable for self-assessment and a great motivation for their participation.

Key Findings

The results of the GLORY registry describe a broad range of practice patterns. However, the steering committee feels that the following key findings from these data are important to highlight:

• Primary THA and TKA are safe surgical procedures, with very low mortality and good outcomes in a high percentage of patients. Furthermore, this was consistent throughout a number of hospitals across 13 countries.

• Despite wide practice variations in GLORY, the functional outcomes of the patients appear to have remained relatively consistent. This consistency is observed despite the geographical and surgical variations intrinsic to the GLORY data set.

• The rate of symptomatic VTE is higher than already reported in randomized trials. Although nearly all patients receive VTE prophylaxis, the actual compliance with guidelines[6] is suboptimal. Further education regarding the nature and content of evidence-based guidelines for VTE prophylaxis in THA and TKA patients is therefore required.

• Furthermore, the use of prophylaxis tails off over time, even though patients are still at risk of thrombosis.[6]

• Registries have an important role to play in identifying areas that require healthcare management attention, and they can therefore have a direct effect on clinical practice.

Future Directions

In GLORY, we have noted a number of clinical practices that do not have evidence supporting their effectiveness/safety and therefore should be evaluated in controlled clinical trials:

• In 38% of patients (58% of US patients and 14% of patients from other countries), a mechanical modality of prophylaxis was used as well as a pharmacological modality. This practice is likely to be performed because mechanical prophylaxis when added to pharmacological prophylaxis may increase efficacy but is not associated with any increased risk of adverse safety outcomes. The use of mechanical methods immediately following surgery before switching to chemical prophylaxis 1 to 2 days after surgery can potentially minimize the bleeding risk while providing practical and effective prophylaxis. According to the 2004 American College of Chest Physicians (ACCP) guidelines, there are no randomized trials comparing multimodal prophylaxis with single modalities, although this approach is commonly used in major orthopedic surgery.[7] It is therefore important to fully test this hypothesis in the setting of a strictly controlled clinical trial.

• It was interesting to note that of the 117 US physicians participating in GLORY, 101 (86%) gave warfarin for VTE prophylaxis to at least 1 patient, and that 52 (51%) of these targeted an international normalized ratio (INR) of 1.5 to 1.9. This widespread practice is based on physician perceptions for

reduced bleeding risk at no cost to efficacy, but as yet there is no conclusive evidence for or against this approach. Data from Caprini and colleagues[8] suggest that there is improved resolution of deep vein thrombosis in patients with a higher INR (2.0-3.0), although this was not investigated in the GLORY registry. Given the current lack of clarity about the role of low-target INR prophylaxis in orthopedic surgery, it is important that a randomized trial comparing this low-target INR with the recommended and evidence-based INR of 2.0 to 3.0 be conducted in order to evaluate the safety and efficacy of such an approach. It would also be of interest to look at the results found for PE prevention practices if comparing with the American Academy of Orthopaedic Surgeons (AAOS) pulmonary embolism prevention guidelines rather than with the ACCP guidelines.[9]

Furthermore, we have also noted a number of apparent associations that would need to be further tested. Because of the observational nature of GLORY and the potential confounding issues found when data are assessed retrospectively, firm conclusions should not be made until these associations can be examined in controlled clinical studies:

• The use of blood salvage techniques for blood management was seen in 18% of THA and 32% of TKA patients in GLORY. Of these patients, 30% of THA and 14% of TKA patients had the blood washed in the infusion device. It was therefore notable that there appeared to be an increased risk of VTE both in-hospital and post-discharge in patients who received blood salvage compared with those who did not. This potential association between the blood salvage technique, which may induce activation of blood coagulation, and the incidence of VTE needs to be fully investigated in a prospective manner.

• Lower preoperative and postoperative Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Short Form-8 Survey (SF-8) scores were found in patients who developed a VTE when compared with the scores of patients who did not. This finding was consistent for both in-hospital and post-discharge VTE events. The possibility that poor preoperative function predisposes to VTE, and that VTE may lead to worse functional outcome, should be examined further.

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Dr. Cushner is a consultant for sanofi-aventis, Bayer, and Astellas. Dr. Friedman is a consultant for and receives research support from Boehringer Ingelheim and Astellas; he is a consultant for Johnson & Johnson; and he is on the speaker's bureau for sanofi-aventis. Dr. Gallus is a consultant for sanofi-aventis, Bristol-Myers Squibb, Bayer, Progen, Astellas, and GlaxoSmithKline. The other authors report no actual or potential conflict of interest in relation to this article.

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CME Test Answer Sheet and Evaluation Form for "Lessons from the Global Orthopaedic Registry"

Release Date of Activity: September 2010
Expiration Date of Activity for AMA PRA credit: September 30, 2011
Estimated Time to Complete this Activity: 3 hours

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1. In a registry, such as GLORY, what is the study design?
a. A randomized clinical trial
b. A case series
c. A prospective observational multi-site study
d. A retrospective patient record analysis

2. In total hip arthroplasty patients in GLORY, what was the most common surgical approach utilized?
a. Posterior
b. Trochanteric
c. Anterior lateral

3. In total knee arthroplasty patients in GLORY, what was the most common prosthesis fixation method?
a. Cemented
b. Porous
c. Hydroxyapatite
d. Other

4. Which was the most frequently used form of in-hospital prophylaxis in the GLORY registry?
a. Low-molecular-weight heparin
b. Elastic stockings
c. Warfarin
d. Intermittent pneumatic compression

5. What was the median in-hospital prophylaxis duration in the GLORY registry?
a. 3 days
b. 4 days
c. 5 days
d. 6 days

6. More than 75% of THA and TKA patients in GLORY received prophylaxis that was in full compliance with the 2001 ACCP guidelines?
a. True
b. False

7. The incidence of any in-hospital bleeding in THA patients in GLORY was?
a. 0.10%
b. 0.48%
c. 0.68%
d. 0.95%

8.What was the most common specified in-hospital complication in TKA patients in GLORY?
a. Fracture
b. Deep-vein thrombosis
c. Cardiac events
d. Wound infection

9. Which patient group had the highest incidence of deep-vein thrombosis in GLORY?
a. Male THA patients
b. Female THA patients
c. Male TKA patients
d. Female TKA patients

10. Which was the only recommendation for good registry design that was not followed in the GLORY registry?
a. Randomized selection of hospitals/clinics or community-wide collection
b. Standardized disease definitions
c. IRB review and approval of registry protocol at each participating site
d. Reporting of all collected data

Record your answers by circling the appropriate letter:

1. a b c d	6. a b c d
2. a b c d	7. a b c d
3. a b c d	8. a b c d
4. a b c d	9. a b c d
5. a b c d	10. a b c d

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Course Evaluation:
Please evaluate the effectiveness of this activity by circling your choice on a scale of 1 to 5, with 1 the lowest and 5 the highest.

Explain global surgical practice patterns in orthopedic surgery.
1 2 3 4 5

Describe prevalent global prophylaxis regimens currently used in orthopedic surgery.
1 2 3 4 5

Recognize how these different practice patterns can influence clinical outcomes in orthopedic surgery.
1 2 3 4 5

Identify best practice when designing and running a registry.
1 2 3 4 5

Use best-practice guidelines to make informed clinical decisions in orthopedic surgery.
1 2 3 4 5

How do you rate the overall quality of the activity?
1 2 3 4 5

How do you rate the educational content of the activity?
1 2 3 4 5

Compared to activities that you have participated in during the past 6 months, how do you rate the overall quality of this activity?
1 2 3 4 5

Was the information presented fair, objective, balanced, and free of bias in the discussion of any commercial product or service?

____Yes _____No

If not, please describe: _____
_____
_____

Suggested topics for future activities: _____
_____
_____

Suggested authors/faculty for future activities: _____
_____
_____
_____
_____
_____

Improvement in Knowledge, Competency, or Practice

Please indicate if this activity has improved:

1.___ Medical knowledge
2.___Practice-based learning and improvement
3.___Communication & interpersonal skills
4.___Professionalism
5.___Systems-based practice
6.___Patient care

Approximate percentage of patients you manage for the disease addressed by this activity?

___0–20% ___21–40% ___41–60% ___61–80% ___>80%

After participation in this activity, have you decided to change one or more aspects of the treatment of your patients?

____ Yes ____ No

If yes, what changes will you make?
_____
_____
_____
_____
_____
_____

If no, please indicate what <u>barriers</u> you might have encountered:

___Already treating this way
___Time
___Patient non-adherence
___Not on formulary
___Not reimbursable by insurance
___Other (please specify): _____

Please indicate:

How you heard about this activity? ____Mail/Print ____Internet/E-mail ____Live Activity

Would you be willing to participate in post-activity follow-up surveys?

____Yes ____No

Would you be willing to participate in a focus group or teleconference aimed at identifying/creating future educational activities that would improve performance in practice or patient outcomes?

____Yes ____No

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