

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

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 This data set will therefore provide a valuable reference source for current practice but should, of course, be superseded in the future.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 tri-

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

als. 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.

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 registries⁵ (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-

Dr. Warwick is with Southampton University Hospital, Southampton, United Kingdom.

Dr. Agnelli is with Sezione di Medicina Interna e Cardiovascolare, Perugia, Italy.

Dr. Cushner is with ISK Institute for Orthopaedics and Sports Medicine, New York, New York, USA.

Dr. Friedman is with Charleston Orthopaedic Associates, Charleston, South Carolina, USA.

Dr. FitzGerald is with the Center for Outcomes Research, University of Massachusetts Medical School, Worcester, Massachusetts, USA.

Dr. Gallus is with the Department of Haematology, Flinders Medical Centre, Adelaide, Australia.

For correspondence, contact David Warwick, MD, Southampton University Hospital, Southampton, United Kingdom.

Am J Orthop. 2010;39(9 Suppl):29-31. Copyright 2010, Quadrant HealthCom Inc. All rights reserved.

**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 guidelines⁶ 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 colleagues⁸ 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.

AUTHORS' DISCLOSURE STATEMENT AND ACKNOWLEDGMENTS

GLORY is supported by an unrestricted educational grant from sanofi-aventis and is coordinated by the Center for Outcomes Research at the University of Massachusetts Medical School, Worcester, Massachusetts.

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.

REFERENCES

1. Anderson FA Jr. Overview of the Global Orthopaedic Registry (GLORY). *Am J Orthop*. 2010;39(9 Suppl):2-4 .
2. Waddell J, Johnson K, Hein W, Raabe J, FitzGerald G, Turibio F. Orthopedic practice in total hip arthroplasty and total knee arthroplasty: results from the Global Orthopaedic Registry (GLORY). *Am J Orthop*. 2010;39(9 Suppl):5-13.
3. Friedman R, Gallus A, Gil-Garay E, FitzGerald G, Cushner F. Practice patterns in the use of venous thromboembolism (VTE) prophylaxis after total joint arthroplasty—insights from the multinational Global Orthopaedic Registry (GLORY). *Am J Orthop*. 2010;39(9 Suppl):14-21.
4. Cushner F, Agnelli G, FitzGerald G, Warwick D. Complications and functional outcomes after total hip arthroplasty and total knee arthroplasty: results from the Global Orthopaedic Registry (GLORY). *Am J Orthop*. 2010;39(9 Suppl):22-28.
5. Alpert JS. Are data from clinical registries of any value? *Eur Heart J*. 2000;21(17):1399-1401.
6. Warwick D, Friedman RJ, Agnelli G, et al. Insufficient duration of venous thromboembolism prophylaxis after total hip or knee replacement when compared with the time course of thromboembolic events: findings from the Global Orthopaedic Registry. *J Bone Joint Surg Br*. 2007;89(6):799-807.
7. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004;126(3 Suppl):338S-400S.
8. Caprini JA, Arcelus JI, Reyna JJ, et al. Deep vein thrombosis and the level of oral anticoagulation therapy. *J Vasc Surg*. 1999;30(5):805-812.
9. Johanson NA, Lachiewicz PF, Lieberman JR, et al. Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. *J Am Acad Orthop*. 2009;17(3):183-196.