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Complications and functional outcomes after total hip arthroplasty and total knee arthroplasty: results from the Global Orthopaedic Registry (GLORY)

Fred Cushner
ISK Institute for Orthopaedics and Sports Medicine

Giancarlo Agnelli
University of Perugia

Gordon Fitzgerald
University of Massachusetts Medical School, gordon.fitzgerald@umassmed.edu

See next page for additional authors

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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 (Ortho)

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.

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. 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. The study was designed and is coordinated by the Center for 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.

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
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).
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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 | In-Hospital (Post-Surgery Bleeding) | In-Hospital or 3 Month Post-Surgery Bleeding |
| LBWH 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.
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
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**Table VI. Functional Outcomes After THA or TKA, Assessed by Means of the WOMAC and SF-8 Questionnaires, According to Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>WOMAC</th>
<th>SF-8 Mental</th>
<th>SF-8 Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Diff</td>
</tr>
<tr>
<td>THA</td>
<td>2662</td>
<td>42.7</td>
<td>76.6</td>
</tr>
<tr>
<td>TKA</td>
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<td>72.8</td>
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<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
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<td>76.7</td>
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<tr>
<td>Female</td>
<td>3489</td>
<td>42.8</td>
<td>73.3</td>
</tr>
<tr>
<td><em>P</em> value</td>
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<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age &lt; 65 years</td>
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<td>43.2</td>
<td>74.5</td>
</tr>
<tr>
<td>Age ≥ 65 years</td>
<td>3459</td>
<td>45.7</td>
<td>74.6</td>
</tr>
<tr>
<td><em>P</em> value</td>
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<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Home Rehabilitation/</td>
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<td>45.2</td>
<td>75.6</td>
</tr>
<tr>
<td>Other</td>
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<td>43.9</td>
<td>73.1</td>
</tr>
<tr>
<td><em>P</em> value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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. 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.

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. 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. 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.

**Mortality Associated With Venous Thromboembolism**

Pulmonary embolism has been reported to account for approximately 10% of in-hospital deaths, 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 90 days 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.

The mortality rate associated with PE or pulmonary infarction was 0.92%, and that associated with DVT was 0.28%. 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 data, 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 \( P < .0001 \) 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 \( \geq 65 \) 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 \( \geq 65 \) 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 \( \geq 80 \) 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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