

Post-discharge compliance to venous thromboembolism prophylaxis in high-risk orthopaedic surgery

Results from the ETHOS registry

David Bergqvist¹; Juan I. Arcelus²; Paulo Felicissimo³; for the ETHOS investigators*

¹Department of Surgery, Uppsala Academic Hospital, Uppsala, Sweden; ²Department of Surgery, University of Granada, Hospital Virgen de las Nieves, Granada, Spain;

³Department of Orthopaedic Surgery, Hospital Fernando Fonseca, Amadora, Portugal

Summary

Venous thromboembolism (VTE) risk persists for several weeks following high-risk orthopaedic surgery (HROS). The ETHOS registry evaluated post-operative VTE prophylaxis prescribed, and actual VTE prophylaxis received, compared with the 2004 American College of Chest Physicians (ACCP) guidelines in HROS patients. We performed a subanalysis of ETHOS to assess patient compliance with ACCP-adherent prophylaxis after discharge and the factors predicting poor compliance. Consecutive patients undergoing hip fracture surgery, total hip arthroplasty, or knee arthroplasty were enrolled at discharge from 161 centres in 17 European countries if they had received adequate in-hospital VTE prophylaxis. Data on prescribed and actual prophylaxis received were obtained from hospital charts and patient post-discharge diaries. Good compliance was defined as percentage treatment intake $\geq 80\%$ with no more than two consecutive days without treatment. A total of 3,484 patients (79.4%) received ACCP-adherent anticoagulant prescription at

discharge and 2,999 (86.0%) had an evaluable patient diary. In total, 87.7% of evaluable patients were compliant with prescribed treatment after discharge. The most common reason for non-compliance (33.4%) was "drug was not bought". Injection of treatment was not a barrier to good compliance. Main factors affecting compliance related to purchase of and access to treatment, patient education, the person responsible for administering injections, country, and type of hospital ward at discharge. Within our study population, patient compliance with ACCP-adherent thromboprophylaxis prescribed at discharge was good. Improvements in patient education and prescribing practices at discharge may be important in further raising compliance levels in high-risk orthopaedic surgery patients.

Keywords

Compliance, ETHOS registry, orthopaedic surgery, post-discharge venous thromboembolism prophylaxis

Correspondence to:

Prof. David Bergqvist
Department of Surgery, Academic Hospital
SE 75185, Uppsala, Sweden
Tel.: +46 18611 4633
E-mail: David.Bergqvist@surgsci.uu.se

Financial support:

The ETHOS study was sponsored by sanofi-aventis (Paris, France).

Received: July 7, 2011

Accepted after major revision: November 1, 2011

Prepublished online: December 21, 2011

doi:10.1160/TH11-07-0464

Thromb Haemost 2012; 107: 280–287

* Listed in Appendix.

Introduction

The risk for venous thromboembolism (VTE) persists for several weeks following high-risk orthopaedic surgery (HROS) (1, 2). Extended-duration post-operative thromboprophylaxis has been shown to reduce the risk of VTE in high-risk subjects (1, 3–6), and current guidelines on prevention of VTE recommend that patients undergoing HROS receive pharmacological thromboprophylaxis that extends well beyond discharge from hospital (7). There are, however, known difficulties associated with achieving good patient compliance with long-term treatment regimens (8), particularly with those designed to avert or reduce risk for clinical events (9, 10), and patient non-compliance to prescribed treatments is common (11).

Few studies have assessed patient compliance with VTE prophylaxis after hospital discharge suggesting that patients can learn to

self-administer treatments and comply with thromboprophylactic regimens, including those involving injectable therapies (12, 13).

The Evaluation of duration of THromboembolic prophylaxis after major Orthopaedic Surgery (ETHOS) registry was a prospective, multinational, observational study designed to investigate real-world compliance with 2004 American College of Chest Physicians (ACCP) recommendations for providing thromboprophylaxis to orthopaedic surgery patients at high risk for VTE (14, 15). To avoid including patients who received no form of prophylaxis in the study, we evaluated only the post-operative and at-discharge thromboprophylaxis prescribed to inpatients who received effective VTE prophylaxis during hospitalisation after HROS (as judged by the treating physician), and the prophylactic treatment actually received by the patient. This registry included data from 17 European countries, and captured information on the thromboprophylaxis received by more than 4,000 patients. The ETHOS registry showed that ACCP-recom-

mended VTE prophylaxis (ACCP-adherent) was prescribed for ≥ 28 days to approximately 63% of patients undergoing hip surgery (hip fracture surgery [HFS] or total hip arthroplasty [THA]), and for ≥ 10 days to approximately 90% of patients undergoing knee arthroplasty (KA) (15, 16 in this issue).

This subanalysis of the ETHOS study aims to assess patient compliance with ACCP-adherent VTE prophylaxis prescribed at discharge, and to identify predictive factors for poor compliance.

Methods

Patients and study design

The complete methodology of the ETHOS registry – including centre participation, planned sample size, patient eligibility criteria and enrolment, data collection and assessment – has been described in detail previously ([16] in this issue). Briefly, patients from 161 randomly selected orthopaedic wards in 17 European countries were considered eligible at hospital discharge for enrolment in the ETHOS registry if they were aged ≥ 18 years, had undergone HFS, THA, or KA in the previous six weeks, and had received in-hospital prophylaxis.

The day of surgery was considered as day 1 of the study. The total post-operative VTE prophylaxis prescribed (in-hospital plus at-hospital discharge) was obtained from case-report forms collected at hospital discharge (the first patient visit). Patients had to complete a daily diary after hospital discharge and until the next follow-up patient visit (planned 4–6 weeks after surgery; see Suppl. Appendix 1 available online at www.thrombosis-online.com), which provided data on thromboprophylaxis actually received (daily intake of thromboprophylaxis) by patients.

Data were collected on all aspects of VTE prophylaxis prescribed during hospitalisation and at discharge, such as person administering any injectable mode of prophylaxis, any mechanical methods of prophylaxis used, and any reasons for not receiving/taking pharmacological prophylaxis as prescribed (see Suppl. Appendix 1 available online at www.thrombosis-online.com). The ETHOS registry did not collect information on VTE and bleeding outcomes, as this was not an objective of the study. The ETHOS study was conducted in accordance with the Declaration of Helsinki and the Guidelines for Good Epidemiology Practice. Locally appointed ethics committees approved the study research protocol, and informed consent was obtained from all patients.

Compliance evaluation

Information from patient diaries was used to collect data on actual prophylaxis received. Compliance analysis was performed in those patients prescribed with an ACCP-adherent prophylaxis (i.e. thromboprophylaxis as recommended and detailed in the 2004 ACCP guidelines [14]) at hospital discharge, who had evaluable

diary data. The ACCP-adherent anticoagulant prophylaxis was defined as patients receiving a low-molecular-weight heparin (LMWH), unfractionated heparin (UFH), for HFS, fondaparinux, or a vitamin K antagonist (VKA). Patient compliance was calculated as the number of days covered with treatment during the prescription period, over the prescription duration at discharge, expressed as a percentage. Good compliance was defined as a percentage of treatment intake $\geq 80\%$ with no more than two consecutive days without treatment (16). The proportion of patients compliant with post-discharge prescription was evaluated and two-sided 95% confidence intervals (CIs) were calculated. For non-compliant patients with $< 80\%$ treatment intake, the following three categories were assessed: no treatment taken; compliance $< 50\%$; and compliance rates from 50% to $< 80\%$.

The number of days, and reasons for not taking the prophylactic treatment, were extracted from patient diaries, and were recorded overall for non-compliant patients. The investigator was also asked to assess reasons for patient non-compliance, and to specify the main reasons assumed for recorded differences between the VTE prophylaxis prescribed compared with the treatment actually received by the patient (see Suppl. Appendix 1 available online at www.thrombosis-online.com).

Predictors of compliance

The assessment of predictive factors for poor compliance was made by univariate – with Chi square tests – and multivariate analyses – stepwise logistic regression where a p-value of 0.20 was required for entering the analysis and a value of 0.05 for retaining the variable in the model. The odds ratios (ORs) and associated 95% CIs for having a poor compliance were determined.

The variables used in the analyses included the following patient characteristics: age (< 57 years; 57– < 67 years; 67– < 74 years; ≥ 74 years), gender, obesity (body mass index ≥ 30 kg/m²), level of education (1–9 years; 10–12 years; 13–16 years; > 16 years; unknown), employment status (working full or part time; not working), preoperative American Society of Anaesthesiologists Grade status (no chronic condition or mild chronic problems; severe or incapacitating chronic problems), type of surgery, type of prophylaxis at discharge (LMWH without VKA; LMWH with VKA; other injectable without VKA; VKA alone), destination after discharge prescription (home; other), and prescription disposition (self-injection; injection performed by a relative; injection performed by a nurse) for patients receiving an injectable treatment; and hospital characteristics: urban/rural location, private/public funding, teaching hospital, number of interventions performed per year, and country (univariate analysis only).

Patients receiving oral VKA treatment alone ($n = 137$) were excluded from the multivariate analysis only since the prescription disposition relating to self-injection/injection performed by a relative or nurse could not be applied to oral treatment.

Analyses were performed with SAS statistical software, version 8.2 (SAS Institute Inc., Cary, NC, USA).

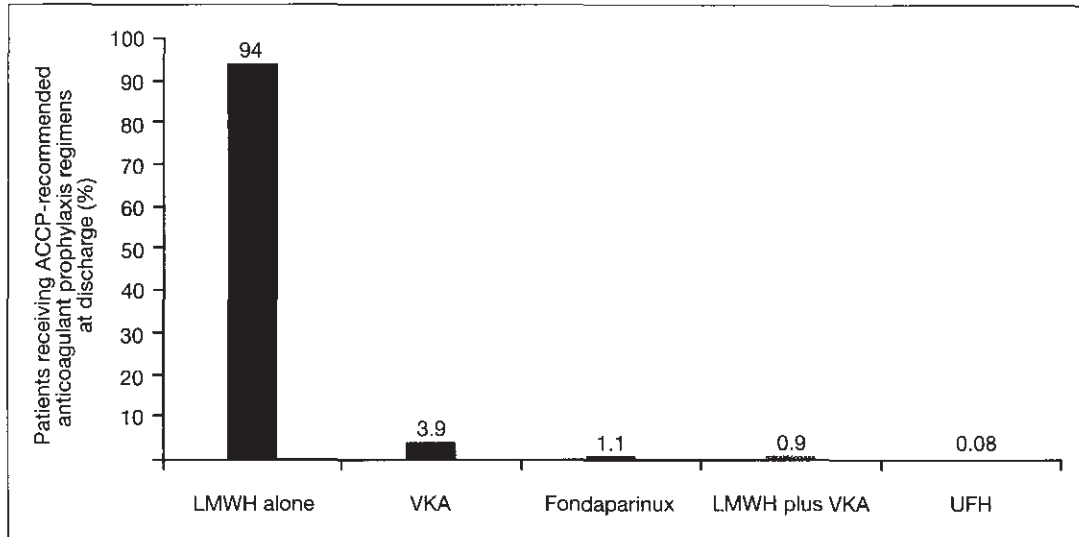


Figure 1: ACCP-adherent anticoagulant prophylaxis regimens prescribed at discharge. ACCP, American College of Chest Physicians; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; VKA, vitamin K antagonist.

Results

Patients

The ETHOS study recruited patients from 161 orthopaedic wards in 17 European countries. In total, 4,388 HROS patients were eligible for the analysis of prophylaxis prescribed (see Suppl. Appendix 2 available online at www.thrombosis-online.com). Patient characteristics have been described previously (15, 16). Briefly, the mean patient age was 65.3 years (± 12.5 years) and 64.8% of patients were female. Total mean hospitalisation duration of patients was 12.7 ± 6.6 days for those undergoing KA, 14.8 ± 6.9 days for those undergoing THA, and 17.8 ± 8.8 days for those undergoing HFS. The majority of patients (84.7%) were discharged home following HROS.

Prophylaxis prescribed at discharge

Among eligible patients, 3,484/4,388 (79.4%) received an ACCP-adherent type of anticoagulant prescription at discharge (see Suppl. Appendix 2 available online at www.thrombosis-online.com).

Among patients prescribed with ACCP-adherent pharmacological prophylaxis, 94% received LMWH monotherapy, 3.9% VKA, 1.1% fondaparinux, 0.9% LMWH plus VKA, and 0.09% received UFH (► Fig. 1). The median duration of prophylaxis prescribed at discharge was 21 days (range, 1–180 days) for both KA and THA, and 30 days (range, 2–60 days) for HFS.

Patient compliance

Among the 3,484 patients considered for the compliance analysis, 2,999 (86%) had an available and evaluable patient diary, whereas 485 (14%) did not (see Suppl. Appendices 1 and 2 available online at www.thrombosis-online.com). For the overall evaluable population analysed for compliance (i.e. those with evaluable diaries; $n = 2,999$), the mean percentage of treatment taken during the prescription period was 91.5% (standard deviation, 18.8). Among the 485 patients with missing diaries, 227 patients (47%) attended the follow-up visit 4–6 weeks after the surgery. According to the investigator, 80% (176/220) of these patients were compliant to the prophylaxis prescribed. The proportion of patients compliant to the prophylaxis prescribed at discharge and the reasons for non-com-

	KA (n = 782)	THA (n = 1,556)	HFS (n = 661)	Total (N = 2,999)
Compliance, n (%)				
Yes	672 (85.9)	1,365 (87.7)	592 (89.6)	2,629 (87.7)
[95% CI]	[83.3–88.2]	[86.0–89.3]	[87.0–91.7]	[86.4–88.8]
Reasons for non-compliance, n (%)				
<80% of treatment intake	105 (13.4)	188 (12.1)	68 (10.3)	361 (12.0)
>2 consecutive days without treatment	5 (0.6)	3 (0.2)	1 (0.2)	9 (0.3)

ACCP, American College of Chest Physicians; THA, total hip arthroplasty; HFS, hip fracture surgery; KA, knee arthroplasty.

Table 1: Compliance with ACCP-adherent anticoagulant prescription and reasons for non-compliance.

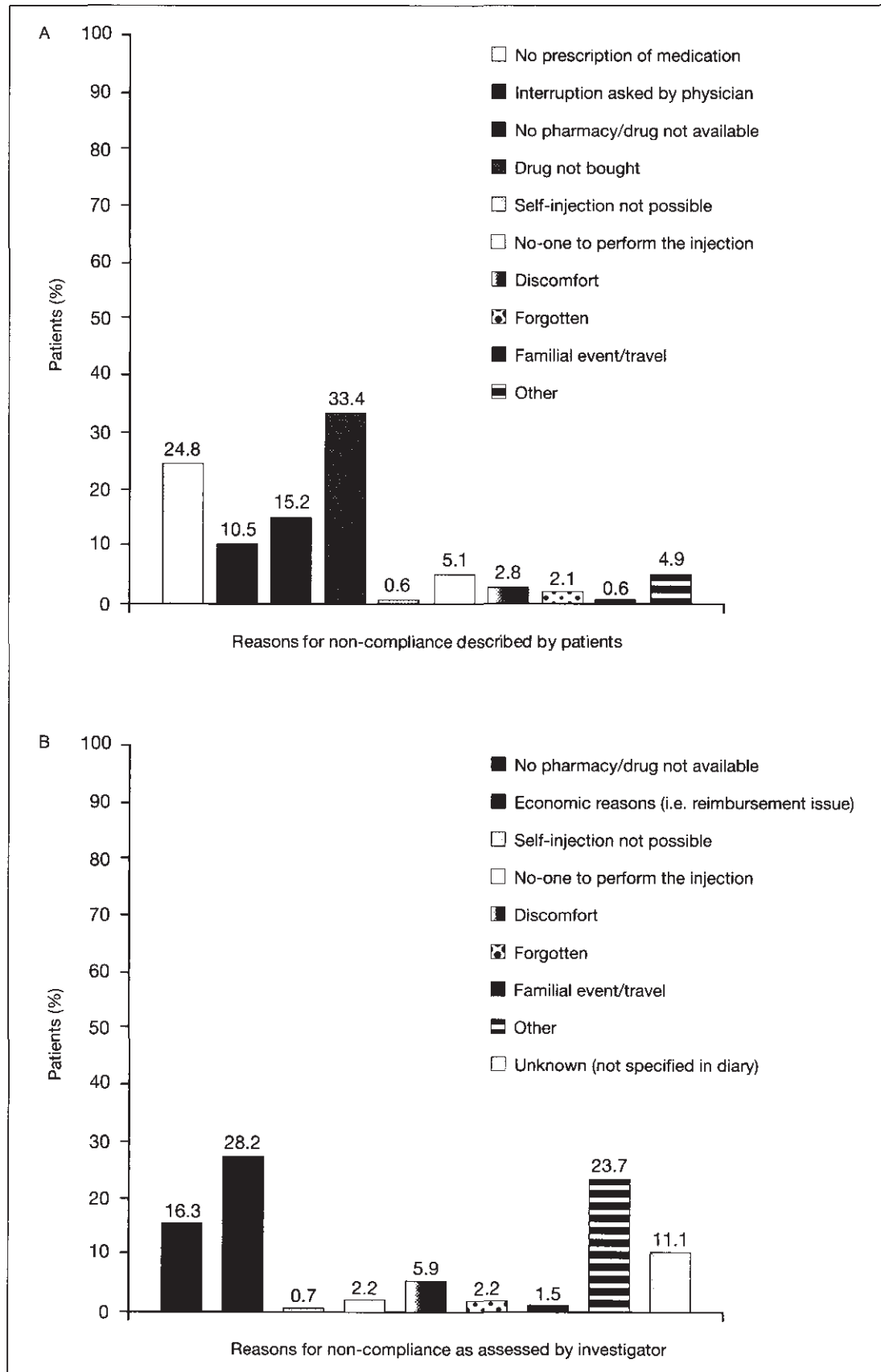


Figure 2: Patient non-compliance. A) Reasons for missing a dose (during the prescription period) in non-compliant patients as reported in patient diary (description of the 1,355 days for which a reason for missing treatment was provided). B) Reasons for patient non-compliance as assessed by the investigator.

pliance are described in ►Table 1. In total, 87.7% (95% CI 86.4–88.8%) of patients that underwent major orthopaedic surgery (n = 2,629) with evaluable diary data were compliant and received ACCP-adherent post-hospital discharge thromboprophylaxis, while 12.3% (n = 370) were non-compliant (see Suppl. Appendix 2 available online at www.thrombosis-online.com).

Among the 12.3% non-compliant patients, in the majority of cases the main reason for failing to meet compliance criteria was treatment intake <80% (n = 361; 12.0%), while in 0.3% of cases (n = 9) the reason for non-compliance was more than two consecutive days with no treatment intake (►Table 1). Among the non-compliant patients defined as those with <80% treatment intake, it was found that 13% had taken no treatment, 26% had taken <50% of prescribed treatment intake, and 61% had taken =50% to <80% of their prescribed treatment intake (see Appendix 2 available online at www.thrombosis-online.com).

Within the total group of non-compliant patients (n = 370), information from patient diaries showed that there were 8,355 days for which a prescription was made. Of these, no intake was recorded in 22% of days, and a reason for missing the treatment was reported in 16% of days. The most common patient-reported reason for missing a daily dose during the prescription period (33.4%) was that the “drug was not bought”. Other main reasons

for missing doses cited by patients were that no prescription was made, or that the drug was not available (►Fig. 2A).

When the compliance was assessed by the investigator, a slightly higher rate of overall compliance was observed compared with the reported patient compliance (93.5% vs. 87.7%, respectively). Furthermore, investigators reported different reasons for non-compliance compared with those reported by patients. The main reasons for non-compliance as defined by investigators were economic/reimbursement reasons (28.2%), and that there was no pharmacy and/or that drug was unavailable to patients (16.3%) (►Fig. 2B).

Univariate and multivariate analyses: predictors of compliance

The univariate analysis showed that compliance with ACCP-adherent thromboprophylaxis was influenced by a number of factors. The level of the patient’s education was found to affect compliance: compliance was lower among patients with longer educations (10–12 years and 13–16 years) compared with those with only 1–9 years of education. Compliance was influenced by the planned

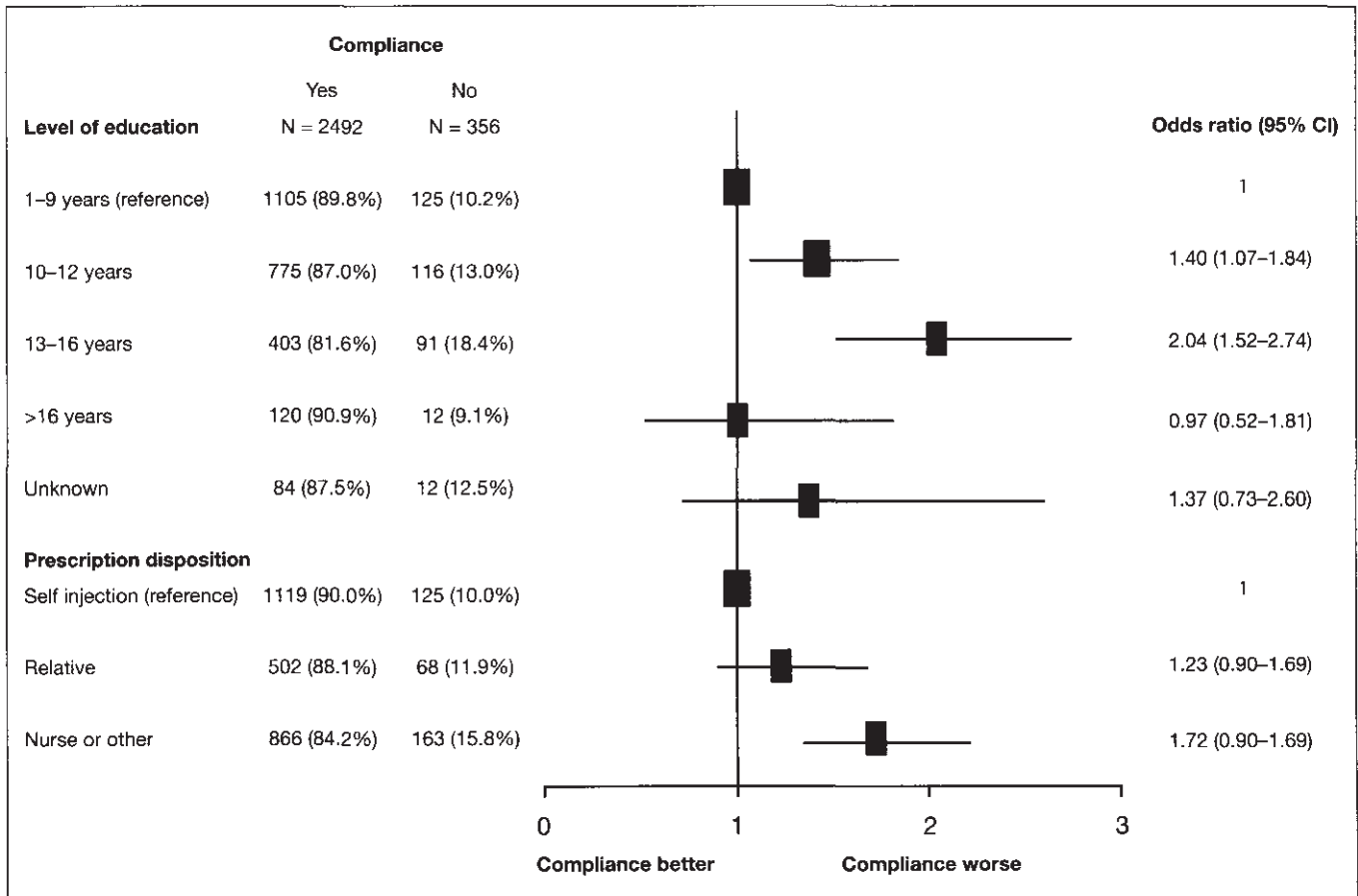


Figure 3: Multivariate analysis of the predictive factors for poor compliance.

management of injections, and was lower when injections were administered by a nurse compared with administration by a relative or by self-injection. The type of hospital ward affected compliance: compliance was lower in patients discharged from hospitals in a rural location (compared with urban), in teaching hospitals, and in hospitals employing a specific VTE protocol during hospitalisation. The univariate analysis found that compliance was not influenced by patient demographics, the type of intervention used, the type of treatment prescribed at discharge (LMWH alone, other injectable alone, VKA alone, or combined LMWH and VKA), the patient destination after discharge, or the level of training given for treatment by injection.

The multivariate analysis showed that predictive factors for poor compliance were secondary school education (10–12 years and 13–16 years; education after age 16 years slightly improved compliance but was still lower than the reference level of primary education, 1–9 years), and injections performed by someone other than the patient (► Fig. 3).

Discussion

The ETHOS registry is the first prospective, observational study in a large cohort of patients who have undergone major orthopaedic surgery to provide “real-life” data on VTE prophylactic practices in European countries (15, 16), and the first to report on patient compliance with post-discharge VTE prophylaxis. In these patients at high risk for VTE, compliance with ACCP-adherent thromboprophylaxis was good, with 87.7% of patients with available diary information taking >80% of the medicines prescribed to them following their discharge from hospital. The study also noted that even among patients with missing diary information, 50% at-

tended their four- to six-week follow-up visit after surgery, and while this group was excluded from the analysis reported here, compliance with prophylaxis in these patients was good, at 80%.

In the group of non-compliant patients, the main reasons identified by patients and investigators for not complying with the prescribed treatment were that the “drug was not bought” and “economic reasons” or that there was “no pharmacy/drug not available”. This suggests that differences in the availability of VTE prophylaxis may be partly due to the reimbursement policies of countries included in the ETHOS study. In the analysis reported here, among the patients in ETHOS who were prescribed an ACCP-adherent regimen at discharge, compliance was generally good across the participating countries (► Fig. 4) despite the fact that there are known to be great country-to-country differences in the level of compensation by health insurances for guideline-recommended injectable therapies, such as the LMWHs (the most commonly used form of prophylaxis in ETHOS – prescribed to 94% of patients).

Only a small proportion of patients were non-compliant because of “discomfort” or “self-injection not possible”. This suggests that the prescription of an injectable treatment for long-term prophylaxis after hospital discharge is not a factor limiting patients’ compliance with VTE prophylaxis. This finding challenges a generally held assumption that patients will always prefer to take an oral medication over a parenteral therapy. In fact, there is evidence that physicians’ perceptions of how patients view, and would accept, injectable therapies may not be in accordance with patient perceptions (17). Studies have shown that patients generally perceived the potential value of effective injectable therapy as an alternative to oral medications positively, particularly if recommended to them by their physicians, and when they understand that the benefits of therapy outweigh any potential drawbacks associated with its administration (18, 19). Indeed, the results from ETHOS

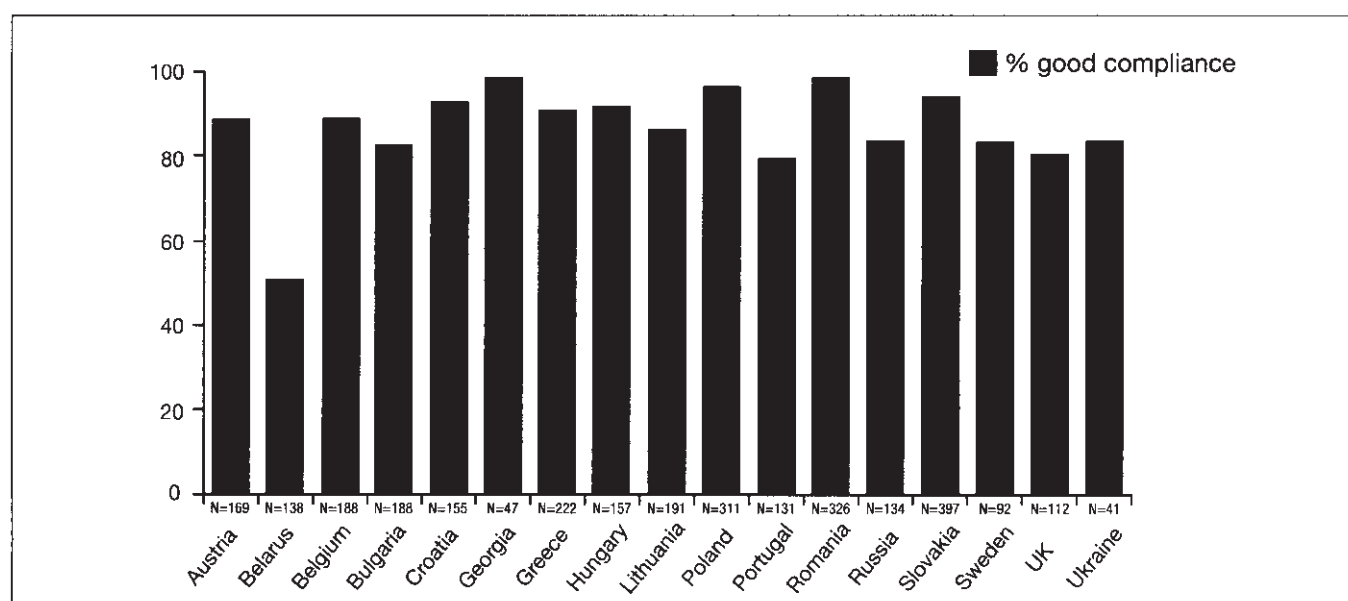


Figure 4: Prophylaxis received after discharge: compliance with discharge prescription per country.

What is known about this topic?

- Current guidelines of venous thromboembolism (VTE) prevention recommend that patients undergoing high-risk orthopaedic surgery (HROS) receive pharmacological thromboprophylaxis that extends well beyond discharge from hospital.
- However, there are known difficulties associated with achieving good patient compliance with long-term treatment regimens, and patient non-compliance to prescribed treatments is common.
- Few studies have assessed patient compliance with VTE prophylaxis after hospital discharge.

What does this paper add?

- In HROS patients, compliance with ACCP-adherent thromboprophylaxis was good, with 87.7% of patients with available diary information taking >80% of the medicines prescribed to them following their discharge from hospital.
- Only a small proportion of patients were non-compliant because of "discomfort" or "self-injection not possible", suggesting that the prescription of an injectable treatment for long-term prophylaxis after hospital discharge is not a barrier to good compliance.
- The main reasons for non-compliance related to purchase and access to treatment.
- Factors influencing compliance included level of patient education, the person responsible for administering injections, country, and type of hospital ward at discharge.

suggest that compliance with injectable therapy is actually better when patients are responsible for self-administering treatment rather than reliant on nurse or clinic visits for injections, or injections given by family members.

The importance of physician recommendation and support for the practice of VTE prophylaxis is known to be of key importance. A recent database study has shown that bleeding, deep-vein thrombosis and pulmonary embolism, arising after TKA were all independent predictors for death, stressing the importance of preventing these events in this patient population (20). In the ETHOS analysis reported here, where patients were prescribed ACCP-adherent thromboprophylaxis, some of the recorded patient non-compliance may have been related to the prescribing physician not agreeing with existing guidelines and therefore not counselling the patient appropriately, or not ensuring their compliance with regimens offering optimal prophylactic efficacy. Interestingly, the inter-country differences in patient compliance were smaller than those observed for the prescription of appropriate prophylaxis when considering both agent and duration (15, 16).

Previous studies of determinants of compliance/adherence with anticoagulant therapies – principally oral anticoagulant warfarin – suggest that non-compliant patients shared distinctive characteristics, including younger age, male gender, no previous experience of a thromboembolic event, feeling burdened by taking therapy, poor understanding of the risks of VTE, and dissatisfaction with the reason for the prescription or with their physician (21). This study found that the level of patient education, the type

of hospital ward from which the patient was discharged, and the country all influenced patient compliance. The impact of patient education levels on compliance appears complex. The lowest compliance was observed in those with a secondary education, yet compliance among subjects with higher education (beyond secondary level) was still less than might be expected based on differences between patients with basic primary versus secondary education (22, 23). A recent study assessing the factors that may be associated with lower or higher compliance rates in patients receiving warfarin, found that education beyond high school was associated with poor compliance. The authors suggest that this result may be linked to more independent decision making in higher educated subjects or to decreased trust in physicians in these patients relative to less educated subjects (24).

There are some study limitations to this ETHOS analysis. Not all European countries took part in the ETHOS registry. ETHOS was designed before data from the ENDORSE survey were available; therefore under-use of appropriate VTE prophylaxis during hospital stay in surgical patients was not assumed and was not assessed. Of the 485 patients with missing diaries, almost 50% attended the follow-up visit 4–6 weeks after the surgery. Although these patients were excluded from the compliance analysis, the investigators' assessment of this patient group showed that up to 80% were compliant, and therefore data relating to these patients' experiences may have been valid for inclusion in our analysis. Some patients who were prescribed a short duration of prophylaxis at discharge may have subsequently received a repeat prescription from their family practitioner. Therefore they may have received an adequate duration of thromboprophylaxis as recorded in the patient diary, without this being captured in the discharge prescription. The sample size, and method of self-assessment/recording of compliance with prescribed prophylactic medication may not facilitate the comparison of our findings with other studies.

In conclusion, ETHOS highlights that in "real-life" practice, among patients discharged with ACCP-adherent thromboprophylaxis, compliance with therapy was good, with 87.7% of patients taking more than 80% of the medicines prescribed. The majority of patients were prescribed injectable thromboprophylaxis, and the study found that injection of treatment was not a barrier to good compliance. The main reasons for non-compliance related to purchase and access to treatment and factors influencing compliance included level of patient education, the person responsible for administering injections, country, and type of hospital ward at discharge. In this study, improvements in patient education and in discharge prescribing practices may be important in ensuring more patients comply with guideline-adherent VTE prophylaxis.

Acknowledgements

This study was sponsored by sanofi-aventis (Paris, France). The authors acknowledge Marinella Calle, PhD, of Excerpta Medica, for medical writing and editorial assistance in the preparation of the manuscript, including copyediting and styling of the manuscript for journal submission. Editorial support was funded by sanofi-aventis.

Conflict of interest

None declared.

Appendix

The following investigators recruited patients (principal investigator in bold): Austria—**Erich Minar**, Wolfgang Hochdaninger, Alfred Ungersböck, Friedrich Kroath, Gerhard Kaltenecker, Hans Krönigsberger, Josef Hochreiter, Martin Krismer, Norbert Freund, Oskar Kwasny, Peter Bösch; Belarus—**Siarhei Zaretski**, Ivan Minakouski, Alexey Maslov, Yuri Kos, Pavel Krasenkov, Yuri Azarov, Sergej Kisel, Viktor Klochkov, Vladimir Tsarev; Belgium—**Johan Bellemans**, Eric Meire, Rudi Pyls, Georges de Brouckère, Jean Colinet, Philippe Kinzinger, Herman Eelen, Johan Bogaert; Bulgaria—**Peter Tivchev**, Chavdar Shokov, Peter Braetov, Dian Enchev, Valentin Ivanov, Nikolay Tivchev, Pavel Mishev, Panayot Tanchev, Atanas Atanasov, Plamen Nenov, Diko Boshnakov; Croatia—**Vladimir Zmak**, Tedi Cicvaric, Branko Tripkovic, Damir Kaplan, Miroslav Gluhinic, Antun Maricevic, Vladimir Boschi, Zvonimir Lovric, Aleksandar Nagy, Dragutin Bitunjac, Zoran Aleksijevic; Georgia—**Nikoloz Avazashvili**, Vazha Gaprindashvili, Tornike Nozadze, Zurab Avazashvili, Levan Teneishvili; Greece—**Kostantinos Malizos**, George Diakos, Theodoros Tsarouchas, Ioannis Krasoulis, George Kehagias, Antonios Asimakopoulos, Chris Dimitriou, Panagiotis Megas, Georgios Skouteris, George Kapetanos, Dionysios Verettas; Hungary—**Kálmán Tóth**, Endre Lénárt, István Zách, István Szigeti, Tamás de Jonge, Tamás Moser, Tamás Gilicze; Lithuania—**Manvilis Kocius**, Robertas Mikalauska, Valdas Maciulis, Rimantas Tarasevicius, Vytautas Mockus, Alfredas Smailys, Manvilis Kocius, Filibertus Taucius; Poland—**Dariusz Chmielewski**, Andrzej Górecki, Krzysztof Czeka, Krzysztof Mocko, Marek Wieczorek, Emil Taszkow, Marek Dolinski, Ireneusz Kotela, Jacek Majewski, Piotr Jeske, Zbigniew Wieczorek, Stanislaw Dawcewicz, Julian Dutka, Andrzej Kozłowski; Portugal—**Paulo Felicissimo**, Antonio Rodrigues, Herminio Loureiro, Abel Trigo Cabral, Antonio Meireles, Jacinto Loureiro, Jorge Mineiro, Rogério Palma Rodrigues; Romania—**Dinu Antonescu**, Ovidiu Alexa, Remus Caranfil, Radu Malancea, Ioan Baier, Dan Cristian Grecu, Nicolae Gogulescu, Tiberiu Bataga, Dan Poenaru, Alexandru Pop, Dan Osvaíd Lucaciu, Călin Tudor Hozan; Russia—**Anatoly Lazarev**, Igor Deev, Anatoly Bondarenko, Afanacy Peshkov, Joulia Ipatko, Sergey Abrosimov, Oganeg Oganesyanyan, Sergey Ivanov, Pavel Zhukov, Anton Starkov, Pavel Boltsev, Ivan Vasin, Sergey Klushkin, Oleg Bogatyrev, Sergey Maslennikov, Andrey Milyukov, Fedor Lazko, Igor Lushnikov, Temur Kvetenadze, Alexander Kostyanov, Yuri Ezhov, Vladimir Ivanov, Anatoly Tyurchin, Stanislav Linnik; Slovakia—**Miroslav Bdzoch**, Jan Cerny, Karol Gottschal, Martin Hromec, Andrej Hudec, Marek Ozorak, Peter Simko, Boris Steno; Sweden—**David Bergqvist**, Sari Ponzer, Björn Edshage, Annika Kragh-Ekstam, Ingemar Olsson; United Kingdom—**Ian Jeffery**, Mohammad Maqsood, Dand Shardlow, Sohail Quraishi, Arpit Patel, Ronan Banin, Ivan Brenkel, Edward Crawford, Peter Kay, Peter Cnudde, Riad Adam; Ukraine—**Oleksandr Kosaykov**, Vladimir Gavrilov, Oleg Drobotun, Yaroslav Linko, Andriy Pidlisetsky, Yaroslav Vasylychshyn, Olena Shevchenko, Andriy Gerasyenko, Olexandr Polyvoda, Valeriy Vakulenko, Igor Shishka, Olexandr Loskutov, Gennadiy Olinichenko, Myckaylo Arshulik, Igor Spesiviy.

References

- Bergqvist D, Benoni G, Björgell O, et al. Low-molecular-weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med* 1996; 335: 696–700.
- 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: 799–807.
- Planes A, Vochelle N, Darmon JY, et al. Risk of deep-venous thrombosis after hospital discharge in patients having undergone total hip replacement: double-blind randomised comparison of enoxaparin versus placebo. *Lancet* 1996; 348: 224–228.
- Comp PC, Spiro TE, Friedman RJ, et al. Prolonged enoxaparin therapy to prevent venous thromboembolism after primary hip or knee replacement. Enoxaparin Clinical Trial Group. *J Bone Joint Surg Am* 2001; 83-A: 336–345.
- Huo MH, Muntz J. Extended thromboprophylaxis with low-molecular-weight heparins after hospital discharge in high-risk surgical and medical patients: a review. *Clin Ther* 2009; 31: 1129–1141.
- Hull RD, Pineo GF, Stein PD, et al. Extended out-of-hospital low-molecular-weight heparin prophylaxis against deep venous thrombosis in patients after elective hip arthroplasty: a systematic review. *Ann Intern Med* 2001; 135: 858–869.
- Geerts WH, Bergqvist D, Pineo GF, et al. American College of Chest Physicians. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; 133 (6 Suppl): 381S–453S.
- Loghman-Adham M. Medication noncompliance in patients with chronic disease: issues in dialysis and renal transplantation. *Am J Manag Care* 2003; 9: 155–171.
- Sackett DL, Haynes RB, Gibson ES, et al. Patient compliance with antihypertensive regimens. *Patient Couns Health Educ* 1978; 1: 18–21.
- Rudd P. Compliance with antihypertensive therapy: raising the bar of expectations. *Am J Manag Care* 1998; 4: 957–966.
- Larsen J, Stovring H, Kragstrup J, et al. Can differences in medical drug compliance between European countries be explained by social factors: analyses based on data from the European Social Survey, round 2. *BMC Public Health* 2009; 9: 145.
- Watts AC, Howie CR, Simpson AH. Assessment of a self-administration protocol for extended subcutaneous thromboprophylaxis in lower limb arthroplasty. *J Bone Joint Surg Br* 2006; 88: 107–110.
- Coilwell CW, Jr., Pulido P, Hardwick ME, et al. Patient compliance with outpatient prophylaxis: an observational study. *Orthopedics* 2005; 28: 143–147.
- 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.
- Bergqvist D, Arcelus JI, Felicissimo P. Evaluation of duration of thromboembolic prophylaxis after major orthopedic surgery: the ETHOS registry. *J Thromb Haemost.* 2009; 7 (Suppl 2): Abstract OC-TU-019.
- Bergqvist D, Arcelus JI, Felicissimo P, ETHOS Investigators. Evaluation of the duration of thromboembolic prophylaxis after high-risk orthopaedic surgery: the ETHOS observational study. *Thromb Haemost* 2012; 107: 270–279.
- Karve S, Cleves MA, Helm M, et al. Good and poor adherence: optimal cut-point for adherence measures using administrative claims data. *Curr Med Res Opin* 2009; 25: 2303–2310.
- Horne R, Cooper V, Fisher M. Initiation of therapy with a subcutaneously administered antiretroviral in treatment-experienced HIV-infected patients: understanding physician and patient perspectives. *AIDS Care* 2008; 20: 1029–1038.
- Horne R, Kovacs C, Katlama C, et al. Prescribing and using self-injectable antiretrovirals: how concordant are physician and patient perspectives? *AIDS Res Ther* 2009; 6: 2.
- Guijarro R, Montes J, San Román C, et al. Venous thromboembolism and bleeding after total knee and hip arthroplasty. Findings from the Spanish National Discharge Database. *Thromb Haemost* 2011; 105: 610–615.
- Arnsten JH, Gelfand JM, Singer DE. Determinants of compliance with anticoagulation: A case-control study. *Am J Med* 1997; 103: 11–17.
- Kulkarni SP, Alexander KP, Lytle B, et al. Long-term adherence with cardiovascular drug regimens. *Am Heart J* 2006; 151: 185–191.
- Herlitz J, Tóth PP, Naesdal J. Low-dose aspirin therapy for cardiovascular prevention: quantification and consequences of poor compliance or discontinuation. *Am J Cardiovasc Drugs* 2010; 10: 125–141.
- Platt AB, Localio AR, Brensinger CM, et al. Risk factors for nonadherence to warfarin: results from the IN-RANGE study. *Pharmacoepidemiol Drug Saf.* 2008; 17: 853–860.