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REVIEW ARTICLE

The new guides for deep venous thromboembolic event prophylaxis in elective hip and knee replacement surgery. Are we nearer or further away from a consensus?☆

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Abstract Venous thromboembolism events (VTEs) prophylaxis after elective hip or knee replacement surgery is a subject of controversy. Three sets of guidelines (National Institute for Health and Clinical Excellence (NICE), American College of Chest Physicians (ACCP) and American Academy of Orthopaedic Surgeons (AAOS)) on this topic have recently been updated.

The guidelines have points in common: prophylaxis is necessary; it is recommended to combine mechanical and pharmacological prophylaxis in patients who have suffered a previous VTE, isolated mechanical measures and low molecular weight heparins (LMWH) are effective; the new oral anticoagulants (NOAC) and fondaparinux are effective drugs. There is some consensus in recommending regional anaesthesia, in advising against echography studies in asymptomatic patients, and in the promotion of early mobilisation of the patient.

There is controversy over the most suitable pharmacological treatment and the time of starting, and the duration of this, as well as on vena cava filters (VCF), antiplatelet (AP) drugs, and VTE or bleeding risk factors.

PALABRAS CLAVE
Profilaxis;
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Artroplastia;
Cadera;
Rodilla

Las nuevas guías de profilaxis de enfermedad tromboembólica venosa en artroplastia de cadera y rodilla electivas: ¿Nos acercamos o nos alejamos del consenso?

Resumen La profilaxis de eventos tromboembólicos venosos (ETV) tras artroplastia electiva de cadera o rodilla es un tema controvertido. Recientemente tres guías clínicas sobre este tema (las guías NICE, ACCP y AAOS) han sido actualizadas.

Las guías presentan puntos en común: es necesario de hacer profilaxis; es recomendable asociar profilaxis mecánica y farmacológica en los pacientes que han sufrido un ETV previo; las medidas mecánicas aisladas son efectivas y las heparinas de bajo peso molecular,

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los nuevos anticoagulantes orales y el fondaparinux son fármacos eficaces. Hay cierto consenso en recomendar la anestesia regional, en desaconsejar estudios ecográficos en pacientes asintomáticos y en promover la movilización precoz del paciente.

Hay discrepancias sobre la terapia farmacológica más adecuada y el momento de inicio y duración de ésta, sobre los filtros de vena cava, los antiagregantes y los factores de riesgo de ETV o sangrado.

Introduction

VTEs represent a significant health problem[1] and a major concern after orthopaedic surgery.[2] Although traumatologists have a good knowledge of these complications and appropriate prophylaxis is performed in most cases,[3] VTEs are directly responsible for 1 out of every 4 deaths occurring after hip arthroplasty (HA).[4] Furthermore, the leading cause of death following HA is ischaemic events,[4] indirectly related to postoperative bleeding, which in turn is often related to pharmacological prophylaxis of VTE. Therefore, there is room for improvement in the quality of VTE prophylaxis and researchers constantly offer new alternatives for such prophylaxis.

Traumatologists find themselves in the difficult position of selecting a VTE prophylaxis protocol that balances the risk of VTE with the risk of bleeding, among a growing number of alternatives. Numerous local, national and supranational institutions have conducted reviews of available evidence which have resulted in clinical practice guidelines and recommendations that help surgeons to make the best decisions. Such guides do not always offer similar recommendations.[5]

Recently, 2 of the most popular and comprehensive guides, the one elaborated by the NICE in the United Kingdom[6] and the ACCP[7] have, significantly updated their recommendations. The AAOS has also presented an update of its guide for thromboprophylaxis after elective HA and knee arthroplasty (KA).[8] These guidelines are the result of extensive and complex studies of the available evidence regarding the efficacy and safety of VTE prophylaxis measures which, despite being based on an identical set of available publications, present notable differences.

The purpose of this work is to analyse the recommendations of these 3 guides, compare them, identify the differences between them and attempt to briefly investigate the causes of these discrepancies. This review focuses exclusively on surgical prophylaxis in elective HA and KA, since the 3 guides provide specific recommendations for this group of patients and also because there is more high-quality evidence available on these patients.

The Spanish Society of Orthopaedic Surgery and Traumatology (SECOT) has also developed a clinical guide for VTE prophylaxis through the Thromboembolism Study Group (GET). The latest version of this guide was published in 2007 and an addendum was released in 2009. This guide is not included in the comparison because, given the steady progress taking place in this field, it currently lacks necessary updates. The authors are aware that there is a clear intention by SECOT and GET to update this guide in the near future.

Table 1 shows a simple comparative summary of the recommendations from the 3 selected guides.

Methodology of the new guides for prophylaxis of venous thromboembolic events

The guide from the National Institute for Health and Clinical Excellence

The NICE guide for ''Venous thromboembolism: orthopaedic surgery'' was updated in October 2011[6] as a complement to the clinical practice guide from 2010 on ''VTE prophylaxis in hospitalised patients''.[9] The guide was elaborated by a comprehensive panel of methodologists, epidemiologists, statisticians and physicians who were supported by a supplementary panel of orthopaedic surgeons. As usual, all the authors expressed their financial conflicts of interest and withdrew from the discussion of those issues in which there could be a conflict. The literature analysis method was based on assigning a level of evidence to each study, based on the Scottish Intercollegiate Guidelines Network (SIGN) system[10] and was followed by a networked meta-analysis with Bayesian hierarchies[11] to establish recommendations.

The NICE guide does not establish priorities or levels in its final recommendations, but instead uses simple terms to express which must be the clinical practice standards with regard to the topic at hand, according to the authors. These consensus recommendations among the authors become the basis for healthcare quality assessment in the UK and are examined specifically.

The guide of the American Academy of Orthopaedic Surgeons

The AAOS guide for ''Prevention of thromboembolic disease in patients undergoing hip and knee arthroplasty'' was published in September 2011[8] as an update of the previous guide from 2007. The guide was elaborated by a panel of methodologists, epidemiologists, statisticians and traumatologists. Key decisions about which studies to include and the final recommendations were specifically subject to the approval of non-physician authors. None of the authors had any financial conflicts of interest and, in addition, intellectual conflicts of interest[12] were also taken into account. Briefly, these consist in authors of a previous study or recommendation having conflicts when objectively evaluating their validity. The method of literature analysis was based on individually assessing the specific results of each study in 2 areas: first, quality was assessed as a measure of the internal validity of each study. This was evaluated according

Table 1 Summary of the recommendations of the three guides (AAOS, NICE and ACCP).

	AAOS guide	NICE[a] guide	ACCP guide
Use of routine eco-Doppler for the postoperative screening of VTE	Discouraged (strong)		Discouraged (1B)
Early mobilisation of patients	Recommended (consensus)	Recommended	Walking within the first 48 hours after surgery is considered as a risk factor for VTE
Use of mechanical or pharmacological prophylaxis	The use of either or both measures is recommended (moderate)	The use of both is recommended	The use of either is recommended • Mechanical (1C) • Pharmacological (1B) • Both (2C)
Type of mechanical prophylaxis recommended	The most adequate type is not recommended (not conclusive)	Anti-embolism stockings, plantar compression, pneumatic intermittent compression devices	Pneumatic intermittent compression devices (1C)
Type of pharmacological prophylaxis recommended	The best option is not recommended (not conclusive)	LMWH, fondaparinux, ribaroxaban, dabigatran	LMWH better than fondaparinux, apixaban, rivaroxaban or dabigatran (2B) LMWH better than aspirin or VKA (2C)
Start of pharmacological prophylaxis	Discussion with patients (not conclusive)	Start after surgery	Start either 12 h before or 12 h after surgery (1B)
Duration of pharmacological prophylaxis	Discussion with patients (consensus)	28–35 days in HA 10–14 days in KA	10–14 days (1B) Extend until 35 days (2B)
Prophylaxis in patients at high risk of VTE	Association of mechanical and pharmacological thromboprophylaxis (Consensus)		
Prophylaxis in patients with high risk of bleeding	Suspension of AP agents (moderate) Only mechanical thromboprophylaxis (consensus)	Suspend contraceptives or hormone replacement therapy 4 weeks before. Consult suspension of AP agents. Discontinue use of pharmacological prophylaxis except if the risk of VTE is greater than the risk of bleeding	Use mechanical measures or no measure (2C)
Type of anaesthesia	Neuraxial anaesthesia is recommended (moderate)	Regional anaesthesia is recommended	
Vena cava filters	Not recommended (not conclusive)	Only in patients with a very high risk of VTE and impossibility to use mechanical and pharmacological prophylaxis	Discouraged in all patients

[a] The degrees of strength of each recommendation are expressed in brackets (the NICE guide does not establish grades of recommendation).

to the criteria of the GRADE working group.[13] Next, applicability was assessed as a measure of the external validity of the results. This was evaluated using the criteria of the PRECIS instrument.[14] Once this was done, a sophisticated network meta-analysis was carried out to establish recommendations. Unusually, in this analysis the weight of VTE with scarce direct clinical relevance (such as distal deep vein thrombosis [DVT] or cases of asymptomatic DVT diagnosed by ultrasound or venography) was reduced and only those events which clearly posed a risk for the lives or limbs of patients (such as pulmonary embolism [PE]) were significantly taken into account. This ''naturalistic'' approach

concentrated on evaluating the effectiveness of an intervention from a clinical point of view, focusing more on those effects which significantly affected patients, than on findings from tests with questionable clinical relevance.

This guide decided to establish 4 levels of strength in its final recommendations: strong, moderate, weak and consensus. This last category had the least strength and was selected when the recommendation was provided based on expert opinion and only for procedures which met the following characteristics: having a low economic cost, not putting patients at risk and being considered as common clinical practices. In addition, it was also necessary that failure to carry out this recommendation could endanger the life or integrity of patients.

The guide of the American College of Chest Physicians

The guide from the ACCP for the ''Prevention of venous thromboembolic events in patients undergoing orthopaedic surgery: antithrombotic therapy and prevention of thrombosis'' was published in February 2012 and represents its ninth version.[7] The ACCP guidelines on thromboprophylaxis are generally considered as the ''bible'' of clinical guidelines for the prevention of VTE. As in previous editions, the methodology consisted in gathering a group of experts who reviewed the literature, stratified studies according to their quality (following the GRADE system[13]) and provided recommendations based on the weight of available evidence. These recommendations have a force which was established according to the ACCP grading system.[15]

ACCP guides have always represented a standard regarding the methodology used to arrive at recommendations and have all proven to be pioneers in applying the techniques of evidence-based medicine (EBM). In this edition, the guide has continued the tradition of rigor and innovation and has been very careful to control intellectual conflicts of interest by placing methodologists at the head of the various committees, as well as attempting to apply the GRADE work group criteria with outmost rigor in the selection and evaluation of studies.[13]

In addition, each group included a relevant physician who was not involved in thrombosis research. Finally, the weight given during the analysis to asymptomatic thrombotic events was fully reassessed, since these have no direct significance for patients, but in previous years they were weighed with equal importance to symptomatic events. In general, all these modifications led to the available evidence being considered of lower quality than in previous editions.

Recommendations on the use or not of prophylaxis (Table 1)

The 3 guides unanimously recommend the use of some form of prophylaxis in patients undergoing elective KA or HA. This recommendation is established with moderate strength in the AAOS guide and with level 1 (B or C) in the ACCP guide. The NICE guide provides no strength levels for its recommendations. The absence of a strong recommendation by the AAOS is specifically based on the fact that the guide does not consider the presence of DVT as a critical event in itself, since it does not jeopardise the lives or limbs of patients directly. In any case, the 3 guides do endorse what is already common practice around the world[3]: some form of prophylaxis must be employed. However, as commented below, discrepancies on the specific type of prophylaxis to be used are general.

Regarding the possibility of associating mechanical and pharmacological procedures, the NICE guide directly recommends the use of a combination of both, while the ACCP guide establishes this association with somewhat lower strength, degree 2B, mainly due to the methodological shortcomings of existing trials, although these suggested that the combination of both procedures may reduce the risk of VTE by 70%.[16] As in many of its other recommendations, the AAOS guide expresses its initial recommendation in an intentionally vague manner: it recommends the use of mechanical and/or pharmacological methods with moderate strength. It only establishes a specific recommendation on the association of both thromboprophylaxis strategies for patients who have suffered a prior episode of VTE and with the lesser degree of force, a consensus, indicating that, although there is no evidence to recommend it, its use seems reasonable in this group of patients with notably increased risk of suffering a new VTE.

Recommendations on the use of mechanical prophylaxis

The 3 guides recommend using mechanical measures for the prophylaxis of venous thromboembolic events. Mechanical prophylaxis systems offer a priori a method to reduce VTE without increasing the risk of bleeding, so they are considered attractive. In general terms, there are 3 main groups of mechanical prophylaxis measures for VTE: compression stockings, intermittent mechanical compression systems and plantar pressure pumps.[17] The NICE guide recommends their use from the time of admission until the patient is capable of walking normally, based on its recommendations from 2010 for bedridden patients.[9] This guide does not set specific differences in its recommendations, given the multiplicity of variables existing even within the same group; nevertheless, it considers that the use of intermittent compression systems and the use of systems reaching up to the thigh could offer benefits. Furthermore, the guide also mentions contraindications for the use of compression stockings (for patients with peripheral arterial disease, skin frailty or lesions or those suffering from heart failure) and the need to use them most of the day in the manner specified by the manufacturer. The ACCP guide only recommends the use of portable intermittent compression devices (PICD), placed in an appropriate manner and for at least 18 hours a day. This is because the available evidence for the remaining systems is considered insufficient. Due to its emphasis on assessing the effect of prophylactic measures only for ''critical'' events, the AAOS guide excluded from its analysis most of the studies used by the other 2 groups[18–23] (in which no deaths or PE took place in any case). Therefore, it does not provide specific recommendations on the type of mechanical prophylaxis to be used, but recommends them in general due to the low risk that their use entails.

Table 2 Risk factors for VTE after KA or HA (those appearing in at least 2 guides are shown in bold).

AAOS guide	NICE guide	ACCP guide
Previous VTE	Previous VTE	Previous VTE
	Age > 60 years	Age
	Significant medical comorbidities	Significant medical comorbidities
	BMI > 30 kg/m^2	BMI > 25 kg/m^2
	Varicose veins with phlebitis	Varicose veins
	Active cancer or in treatment	Cardiovascular disease
	Admission to ICU	Walking within the first 48 h after surgery
	Dehydration	
	Known thrombophilia	
	First-degree family history of VTE	
	Hormone replacement therapy	
	Oestrogen contraceptives	

Recommendations on the use of pharmacological prophylaxis

The type of drug prophylaxis to be used is one of the most interesting topics for the readers of these guidelines. The 3 guides agree that *LMWH, fondaparinux and NOAC are appropriate medications for the prophylaxis of VTE*. Once again, the similarities end there, since each guide has specific criteria for recommending one or the other and they also differ in their assessment of the role in prophylaxis of aspirin, unfractioned heparin (UFH) and vitamin K antagonists (VKA).

The 3 guides recommend the use of low molecular weight heparin for prophylaxis of venous thromboembolic events. All the guides used LMWH therapy (especially enoxaparin) as a comparator of the effectiveness of other prophylaxis strategies in their analysis of effectiveness, along with placebo when available. Neither the NICE guide nor the AAOS guide establishes differences in their recommendations over other recommended drug therapies (dabigatran, fondaparinux and rivaroxaban in the NICE guide, and also aspirin and VKA in the AAOS guide). The ACCP guide is the only one which recommends the preferential use of LMWH versus NOAC, fondaparinux or UFH (grade 2B recommendation), as well as aspirin or VKA (grade 2C recommendation). This decision is established for UFH because one meta-analysis of data from studies without direct comparison suggested an added reduction of 20% DVT with LMWH compared to UFH. A particularly marked increase in bleeding events was observed with VKA compared with LMWH, especially in extended regimes. Aspirin seemed as safe as LMWH, but not as effective in preventing asymptomatic DVT. Fondaparinux appeared to be equally effective in preventing VTE, but led to a 1% increase of major bleeding events. The recommendation for the use of LMWH compared to NOAC is established based on the limited information on the safety profile of these new drugs against the well-established profile of LMWH.

Fondaparinux is recommended by the 3 guides as an appropriate drug therapy for the prophylaxis of VTE. The only specific comment is that referred by the authors of the ACCP guide and already mentioned.

All the guides recommended dabigatran and rivaroxaban for the prophylaxis of VTE in these patients. Apixaban, which was commercialised in late 2011, only became available at the time when the ACCP guide was being elaborated, so this guide is the only one recommending it. No specific recommendations are made regarding preferential use among them or compared to other products, except for the already mentioned exception of the ACCP regarding the safety of these recently introduced drugs.

The use of aspirin for prophylaxis of VTE is recommended by the ACCP and AAOS guides. However, the NICE guide explicitly states that ''aspirin or other AP drugs should not be considered suitable drugs for the prophylaxis of VTE''. The inclusion of aspirin as a drug for prophylaxis of VTE is one of the most controversial issues in these guides. Although, as previously noted, the AAOS guide is specifically inaccurate in evaluating the relative efficacy of different agents and establishes that there is a lack of specific evidence to do any more than recommend them as a whole, the recommendation of the ACCP guide is particularly interesting, since it is in direct contrast to the prior guide from 2008,[24] which explicitly discouraged its use with level 1A strength. This change in judgment by the authors is due to an increasingly patient-oriented approach and to the events affecting them in a more ''naturalistic'' clinical setting (as opposed to criteria focusing more on the results of screening tests for asymptomatic VTE). In particular, the positive results for aspirin of an isolated and high-quality study had a significant influence.[25] The recommendation to preferentially use LMWH versus aspirin of the ACCP guide is based on 2 other studies[26,27] which helped the authors of the NICE guide to advise against aspirin as an adequate treatment. In any case, this debate seems far from closed.

The ACCP and AAOS guides recommend the use of VKA for prophylaxis of VTE, while the NICE guide does not consider this therapeutic alternative, regarding it as obsolete. As previously mentioned, the ACCP guide recommends the preferential use of LMWH versus VKA due to its increased safety.

Recommendations on the duration of thromboprophylaxis

In this issue, as in various others, there is no clear consensus. While the AAOS guide does not provide indications on

the duration of prophylaxis beyond recommending that the surgeon should discuss the duration of treatment with the patient, the NICE guide recommends extending prophylaxis from 10 to 14 days after KA and from 28 to 35 days after HA, and the ACCP guide recommends prolonging prophylaxis up to 35 days in both cases (compared to prolonging prophylaxis from 10 to 14 days with level of evidence 2B). The authors of the AAOS guide felt that the available evidence[28] for prolonging therapy came mostly from studies sponsored by pharmaceutical companies and referred to a single drug. Thus, they did not consider that the evidence had sufficient quality. The authors of the ACCP guide, who in the previous edition had made similar recommendations to those of the NICE guide, on this occasion opted for homogenising their recommendations into extended therapy in both KA and HA, based on the same studies which did find a significant reduction of the risk of symptomatic DVT with prophylaxis extended to 35 days.

Recommendations on the time of initiation of thromboprophylaxis

This issue also leads to differences which should be taken into account. While, once again, the AAOS guide makes no recommendations in this respect, the NICE guide recommends postoperative initiation in all cases (after 1–4 h with dabigatran, after 6 h with fondaparinux, after 6–12 h with LMWH or UFH and after 6–10 h with rivaroxaban), and the ACCP guide recommends starting treatment at least 12 h before or 12 h after surgery (as opposed to doing so 4 h before or 4 h after surgery, with level of evidence 1C).

These 2 recommendations have significant implications for everyday clinical practice. First, the NICE recommendation for only postoperative therapy conflicts with the recommendations in the technical specifications for most LMWH, which recommend starting treatment 12 h before surgery. This ''off-label'' recommendation for the use of LMWH is only made taking into account the potential risk of increased bleeding compared with perioperative administration[29] and the fact that concomitant use of mechanical measures is also recommended from the time of admission, that is, from before surgery. It must be borne in mind that this recommendation reflects a systematic postoperative initiation of LMWH therapy, which is an established clinical practice for many surgeons.[29]

Second, the recommendation by the ACCP to not employ prophylaxis in the first 4 h postoperatively clashes with the recommended schedule of implementation of dabigatran (1–4 h after the end of surgery) and is based on significant evidence that early postoperative treatment with LMWH[30,31] and fondaparinux[32] is associated with an increased risk of bleeding, without offering significant advantages regarding VTE prevention.

Recommendations on the use of vena cava filters

Temporary or permanent VCF employed to prevent VTE in high-risk patients in whom prophylaxis by other means cannot be used represent another point of contention in these guides. The NICE guide recommends considering their use in high-risk patients (previous VTE or active cancer) in whom pharmacological or mechanical measures are contraindicated. The AAOS guide chooses not to draw conclusions, given the insufficient evidence available and the ACCP guide advises against their use (as opposed to not employing any prophylaxis) in patients at high risk of bleeding or with contraindication for other types of prophylaxis (grade 2C recommendation). The conclusions of the NICE guide are based largely on a study conducted among hospitalised, non-surgical patients,[33] while the authors of the AAOS guide found no quality evidence to establish even a ''consensus'' recommendation. The authors of the ACCP guide weighed the decreased risk of PE observed in a low-quality meta-analysis[34] against the significant complications resulting from the use of VCF reported in a sizeable observational study[35] and considered that the risks far outweighed the benefits.

Despite the lack of consensus, we must take into account that the circumstances which force patients to consider VCF rarely occur among patients undergoing an elective KA or HA procedure: active cancer, previous VTE, active DVT or sufficiently high risk of bleeding to represent a contraindication for pharmacologic prophylaxis.

Recommendations regarding the screening for venous thromboembolic events

While the NICE guide does not address this issue, both the AAOS guide and the ACCP guide discourage the use of ultrasound techniques in the routine postoperative screening for DVT in asymptomatic patients (with strong and 1B recommendation grades, respectively). Both groups base their recommendations on the fact that the identification (and subsequent treatment) of asymptomatic DVT is not associated with a decreased incidence of symptomatic DVT or PE.[36,37] The authors of the ACCP guide also indicate that patients with asymptomatic DVT suffer more episodes of bleeding when treated with anticoagulants in a prolonged manner.[36,37]

Recommendations for early mobilisation

While the ACCP guide does not provide specific recommendations, *the AAOS and NICE guides recommend early mobilisation of patients as an appropriate strategy to prevent the occurrence of VTE*. The authors of the AAOS guide establish this recommendation as a ''consensus'' because it has a low cost, entails minimal risk for patients and is consistent with everyday clinical practice. The authors of the NICE guide recommend it as a reflection of everyday clinical practice and based on experimental studies suggesting that mobilisation reduces venous thrombosis despite the lack of clinical studies endorsing its use. Curiously, the ACCP guide identifies early mobilisation of patients, defined as walking within the first 2 days postoperatively, as a risk factor for VTE.

Table 3 Bleeding risk factors after KA or HA.

AAOS guide	NICE guide	ACCP guide
Congenital bleeding disorders (such as haemophilia)	Active bleeding	Previous major bleeding
Active liver disease	Acquired bleeding disorders (such as acute liver failure)	Severe renal failure
Use of antiplatelet agents	Use of anticoagulants which increase the risk of bleeding (such as VKA in doses that elevate the INR > 2)	Use of antiplatelet agents
	Spinal interventional procedures performed in the last 4 h or expected within the next 12 h	History of uncontrolled intraoperative bleeding
	Acute stroke	Uncontrolled intraoperative bleeding during the procedure itself
	Thrombocytopenia (<75,000/ml)	Extensive surgical dissection
	Uncontrolled systolic hypertension (>230/120 mmHg)	Review surgery
	Congenital bleeding disorders (such as haemophilia or von Willebrand disease)	

Risk factors for venous thromboembolic events and recommendations for patients at high risk of venous thromboembolic events

Risk factors for suffering a VTE after KA or HA should be clearly defined, since they would enable the identification of a group of patients at increased risk who could benefit from more aggressive prophylactic measures. *The 3 guides agreed in identifying a history of having suffered a previous VTE as a risk factor for suffering a new VTE after KA or HA*. The authors of the AAOS guide restricted their analysis of the importance of other risk factors to studies of KA or HA and found weak evidence in 2 studies (of moderate and low quality)[38,39] that a previous VTE increased the risk of suffering a new VTE by between 4 and 8 times. They found no other potential risk factors. The fact that they could not find evidence of sufficient quality to establish other risk factors is probably due to the significant increase in risk caused by the surgery itself, which could mask minor effects produced by other risk factors. However, in 2010 the authors of the NICE guide conducted a more comprehensive analysis that included studies with other surgical and medical patients and identified a long list of risk factors for VTE (Table 2). They inferred that if these factors were applicable in some populations, they should also be so in patients undergoing KA or HA. The ACCP guide identifies a series of general risk factors for VTE in orthopaedic surgery (Table 2), but agrees with the AAOS guide in assigning them only a relative importance, given the much higher specific gravity of risk associated with the intervention itself.

The NICE guide makes no additional recommendations for patients with these risk factors (except as provided in the section on VCF, above), because it considers all patients undergoing KA or HA as high-risk patients (undergoing an intervention of over 60 min duration, which affects the lower limbs and causes reduced mobility). The AAOS guide recommends (with ''consensus'' grade recommendation, that is, there is no certain evidence, but it is recommended due to low cost, low risk and because it is considered as everyday clinical practice) that a combination of pharmacological and mechanical measures should be used in patients with a previous history of VTE. Finally, the authors of the ACCP guide indicate that the estimation of individual risks for these factors is not safe enough to allow them to make specific recommendations for different risk strata.

Bleeding risk factors and recommendations for patients at high risk of bleeding

Risk factors for increased bleeding after KA or HA should be clearly defined, since they would enable the identification of a group of patients at increased risk who could suffer additional problems derived from the measures for VTE prophylaxis. The 3 guides identify various risk factors which are listed in Table 3. It seems clear that the guides do not agree on the factors selected. The AAOS guide exclusively selected as risk factors severe liver disease, congenital coagulation disorders and the use of AP agents, whilst rejecting others (those included in the NICE guide, for example), considering them as low-quality evidence to make a recommendation. The authors of the NICE guide, however, offer a long list of risk factors for bleeding based on clinical experience and the exclusion criteria of trials. The ACCP guide identifies some general risk factors for bleeding in orthopaedic surgery, but once again downplays them due to the absence of specific risk assessments with sufficient validation in orthopaedic surgery.

For patients with the risk factors described, the authors of the AAOS guide advise the discontinuation of AP agents before surgery (moderate grade recommendation) and recommend, by consensus, the exclusive use of mechanical prophylaxis measures in patients with liver disease or congenital coagulation disorders. The authors of the ACCP guide agree with this recommendation to use only PICD (and no pharmacological prophylaxis) in patients with risk factors with a grade 2C recommendation, but estimates that those subjects with a single risk factor (in particular the use of AP agents) should choose between the discomfort of PICD and the small increase in risk of bleeding which they entail. The NICE guide is somewhat ambiguous in this case, as it

Table 4 Common conclusions between the clinical guides by ACCP, AAOS and NICE.

Conclusions common to the three guidelines for prophylaxis of venous thromboembolic events after knee or hip arthroplasty.

- Patients undergoing elective KA or HA should receive some form of mechanical and/or pharmacological prophylaxis.
- Having suffered a prior VTE is a risk factor for presenting a new VTE after surgery.
- Those patients who have suffered a previous VTE should receive mechanical and pharmacological prophylaxis.
- Intermittent mechanical compression systems are an effective mechanical measure for prophylaxis of VTE after KA or HA.
- LMWH, fondaparinux and NOAC[a] are effective drugs for prophylaxis of VTE after KA or HA.

Conclusions appearing in at least two guides and which are not evaluated by the third guide

- Patients undergoing elective KA or HA must be mobilised early (NICE and AAOS).
- Routine ultrasound screening studies for VTE should not be conducted on asymptomatic patients after KA or HA (ACCP and AAOS).
- It is better to use regional or neuraxial anaesthesia in these patients (NICE and AAOS).

[a] Apixaban is a NOAC which only became available while the ACCP guide was being published and was, therefore, not included in the other two guides.

discourages the use of pharmacological prophylaxis in patients with risk factors, except when the risk of VTE is greater than the risk of bleeding. It recommends discontinuation of contraceptives or hormone replacement therapy 4 weeks before surgery and with respect to the use of AP agents, it recommends consulting with a multidisciplinary team, since the risks of discontinuation of therapy are highly variable and difficult to estimate, depending on the initial reason for using the AP agents.

Recommendations regarding the type of anaesthesia to employ

Both the NICE guide and the AAOS guide (with a moderate grade recommendation) recommend the use of regional anaesthesia techniques as the best alternative to general anaesthesia in patients about to undergo KA or HA. The ACCP guide did not specifically analyse this concept. The authors of the AAOS guide substantiate their recommendation based on the lower risk of bleeding with neuraxial anaesthesia versus general anaesthesia (based on 8 high-quality studies) rather than a reduction in risk of VTE, which they did not observe since they limited their analysis to studies on KA or HA (only 3 studies). The authors of the NICE guide, however, include other studies in their analysis (a total of 15 studies and 1 meta-analysis[40]) not limited to lower limb arthroplasty and conclude that the use of regional anaesthesia techniques reduces the risk of DVT and PE.

Discussion

It is not the intention of the authors, nor is it within their capacity, to draw conclusions from the analysis of the 3 guides and synthesise them into a series of common recommendations. This is the responsibility of SECOT and GET. However, a detailed analysis of the 3 guides leads to some general comments on the form, substance and tone of each.

The NICE guide will surprise traumatologists by its brevity and the cleanliness of its recommendations. After a current and sophisticated analysis of EBM, the authors provide physicians with clear recommendations on what to do with their patients without avoiding controversial issues, offering physicians various options on what treatment to use. The guide lacks a closer inspection of 2 methodological issues which have become important in recent times: the concept of intellectual conflicts of interest and the use of outcome variables with direct impact on the patient (the so-called ''naturalistic'' approach).

The publication of the AAOS guide caused a significant impact within the scientific community interested in thromboprophylaxis. A guide elaborated by ''traumatologists'' offered recommendations which directly opposed those contained in established guides: the isolated use of mechanical means, the use of aspirin, etc. Furthermore, it was somewhat ambiguous in numerous aspects of thromboprophylaxis arguing a lack of quality evidence. As we have seen, a few months later, this same scientific community found that the sacrosanct ACCP guide aligned its recommendations, at least in part, with those in this guide. We must keep in mind that the criticism of its ambiguity is clearly justified: physicians expect practice guides to offer a clear orientation on what to do and this guide rarely offers such clear answers.

The ACCP guide was significantly updated in this edition. The adoption of the GRADE system for the evaluation of studies, the incorporation of the concept of intellectual conflicts of interest and the adoption of a more patient-oriented approach led to a radical change in some recommendations and, in general, reduced the strength of the recommendations established throughout the guide. Its clarity and scientific soundness, as well as the immediate assumption of new perspectives in EBM, enable it to maintain a solid position as the ''bible'' of thromboprophylaxis.

Conclusions

These 3 recent guides provide quality information for physicians to guide decisions about prophylaxis for VTE in patients undergoing elective KA or HA. However, we must take into account that the common points of the 3 guidelines are very scarce (Table 4) and are limited to the need for prophylaxis in these patients: advising an association of mechanical and pharmacological prophylaxis in patients who have suffered a previous VTE, since they are at an increased risk of a new VTE; establishing isolated mechanical measures as effective and considering LMWH, NOAC and fondaparinux as effective pharmacological measures. There also seems to be a partial consensus on regional anaesthesia being preferable to general anaesthesia, on ultrasound screening studies not being necessary in asymptomatic patients and on early mobilisation of patients being recommendable.

There are however, significant discrepancies about which therapy is most appropriate, the use of aspirin as prophylaxis, the ideal time of initiation of drug therapy and its duration, and with regard to the use of VCF, discontinuation or not of AP drugs, which are the risk factors for VTE or bleeding and what attitude to adopt with patients who present them.

Level of evidence

Level of evidence III.

Ethical responsibilities

Protection of people and animals. The authors declare that this investigation did not require experiments on humans or animals.

Confidentiality of data. The authors declare that this article does not reflect any patient data.

Right to privacy and informed consent. The authors declare that this article does reflect any patient data.

Conflict of interests

M.A.R.I. has worked as a paid consultant for Bristol-Myers Squibb Spain. The remaining authors have no conflict of interest to declare.

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