Venous thromboembolism risk stratification and thromboprophylaxis with low molecular weight heparin in patients undergoing major ambulatory surgery: an observational prospective study

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Abstract

Aim: Although supposedly low, the risk of venous thromboembolism (VTE) after major ambulatory surgery (MAS) remains to be established. We have carried out a prospective validation of the risk stratification of VTE in MAS patients.

Methods: 402 consecutive patients were stratified according to a Spanish consensus as: a) no risk of VTE (n=141), b) moderate risk (n=228), and c) high risk (n=33). The moderate and high risk groups received thromboprophylaxis with low molecular weight heparin. On post-operative day 10, a colour Echo-Doppler was obtained; on days 10 and 30 different parameters of efficacy and safety were measured.

Results: 357 patients completed the study. No symptomatic events were observed; one case of asymptomatic deep vein thrombosis was observed. Overall, in 39 patients (three from the low risk group and 36 in the moderate and high risk groups; $p<0.001$) a decrease to 15 cm/s was observed in interior femoral blood flow. Haemorrhagic complications, all of them minor, in the surgical wound accounted for 2%. The study of thrombophilia revealed a high number of patients with hidden thrombophilia (28.1%).

Conclusion: MAS patients are not free of VTE events and require risk stratification. Thromboprophylaxis with LMWH in moderate and high risk of VTE is safe and effective.

Keywords: Major ambulatory surgery; Day case surgery; Venous thromboembolism; Deep venous thrombosis; Risk stratification; Antithrombotic drugs; Low molecular weight heparin; Bemiparin

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Introduction

Venous thromboembolic disease (VTE) is a well known pathology with many repercussions, whose preventive aspect (recommendations) is fairly well established in the field of non-ambulatory surgery [1,2].

Major Ambulatory Surgery (MAS) is now in its maturity and is widely used. Its special characteristics differentiate it from what could be considered traditional surgery, and currently nobody questions its efficacy and safety, although the need for certain actions used in conventional surgery, such as antithrombotic therapy, has been widely debated. In this sense, very few works have been published and there are almost no specific orientations regarding thromboprophylaxis within the field of MAS [3,4]. As a result of the paucity of specific guidelines concerning thromboprophylaxis, there are some variations in clinical practice.

In light of the foregoing, in Spain a panel of experts was created with a view to gaining consensus from the available information about thromboprophylaxis in MAS [5]. The aim of the present work was thus to validate the recommendations made by that panel for MAS procedures in general surgery. In particular, our aims were: a) to confirm the existence of different groups at risk of VTE in MAS (risk stratification) and b) to assess the effectiveness and safety of a low-molecular weight heparin (LMWH) administered in the post-operative period for the prevention of thromboembolic events after general MAS surgery in moderate and high risk groups.

Materials and Methods

The study included 402 consecutive patients who agreed to participate (written consent) in a prospective observational clinical study. The patients were undergoing MAS procedures at the University Hospital in Salamanca (Spain) along a period of 20 months (2007–2008). All interventions were carried out by the same surgical team: two highly experienced senior surgeons.

Basal determinations

Before surgery, the following actions were implemented: a) collection of the clinical history of each patient, placing special emphasis on a previous or family history of thrombosis; b) randomization, for the search for thrombophilia in one third of the patients; c) assessment of the thromboembolic risk of each patient; on stratifying risk, the type of thromboprophylaxis was determined automatically.

Thromboembolism risk stratification

The risk of VTE was determined following the guidelines of the 2006 Spanish Consensus Conference [5]. The combination of surgical (A) and personal (B) risk allowed the patients to be classified in

Table I Evaluation of the risk of VTE and proposal of thromboprophylaxis*.

A. Surgical risk factors	B. Personal risk factors	Risk of VTE	Proposal of prophylaxis
Low	I	No risk	Only physical measures
	2	No risk	Only physical measures
	3	Moderate risk	+ LMWH moderate dose
Moderate	I	Moderate risk	+ LMWH moderate dose
	2	Moderate risk	+ LMWH moderate dose
	3	High risk	+ LMWH high dose
High (No MAS)	I–4	No MAS	

A. Surgical risk factors

Low risk	Moderate risk
Laparoscopic surgery < 60'	Laparoscopic surgery > 60'
Abdominal wall hernias (unilateral)	Abdominal wall hernias (bilateral)
Cholecystectomy	
Perianal surgery	
Extensive soft parts surgery	

1= minimum

2 = low

3 = moderate

4 = high (not candidate for MAS)

B. Personal risk factors

Level 2 (low risk)	Level 3 (moderate risk)
Age < 40 years	Age > 40 years
Pregnancy. Puerperium. Estrogens. Contraceptives	History of VTE
Cardiorespiratory insufficiency	Active neoplasm; chemotherapy
Varicose veins	Chronic myeloproliferative syndrome
Inflammatory intestinal disease	Nephrotic syndrome
Obesity (BMI >30%)	Congenital and acquired thrombophilia
Chronic smokers	Paralysis of lower limb
Orthopaedic surgery of lower limb	
Immobilisation	
Length of surgery < 30 min.	

two groups (Table 1); without risk of VTE, and hence not requiring LMWH, and with the risk of VTE, for whom the administration of LMWH is considered. The latter patients were subdivided into moderate and high risk individuals.

Thromboprophylaxis

All patients were recommended (in oral and written form) to walk actively every day from the day after operation. No elastic stockings were recommended or prescribed. Selectively (depending on the level of risk), Bemiparin (Hibor®, Laboratorios Rovi SA, Madrid, Spain) was administered subcutaneously at doses of 2,500 IU/24 h or 3,500 IU/24 h (the latter in the high risk cases), starting 6 h after the end of surgery and lasting 7 days. Although Bemiparin does not have contraindications at moderate prophylactic doses, in the case of high doses the following were taken into account: platelet count <50,000 mm^3, severe renal impairment that would require monitoring, and active gastro-intestinal ulceration. It was recommended that the point of subcutaneous injection of the LMWH should be as far away as possible from the surgical wound.

Study of thrombophilia

Owing to economic problems, this study was only performed in one third of the patients (pre-operative blood extraction). To accomplish this, a table of random numbers compiled at the start of the study was used. The results were not made available until the final evaluation of the data and hence were not taken into account on assessing the pre-operative risk of VTE and performing the stratification. Indeed, the aim of the study of thrombophilia was precisely to determine how this parameter would influence the stratification *a posteriori* without knowledge of such results (*a priori*).

The following determinations were made: levels of antithrombin-III, protein C and S, presence of Leiden Factor V and FII20210 of prothrombin, levels of homocysteine and determination of Methylene-Tertrahydrofolate-Reductase (MTHFR). Likewise, the existence of resistence to Active Protein C (R-APC) (not Leiden Factor V) was determined. The following were considered pathological: antithrombin-III deficit (< 80%) deficit in protein C and S (<60%), R-APC< 2.5 and hyperhomocysteinaemia > 15 µg/dL.

Follow-up

In all patients, regardless of their risk group, different controls were performed at 10 and 30 days after the surgical procedure. On the 10th day, the following were explored:

1) clinical assessment, searching for symptomatic thromboembolic events and complications derived from the administration of the LMWH, mainly ecchymosis at the injection site and haemorrhages (zone and amount);
2) degree of compliance to the prophylaxis (adherence to the LMWH regime) by the patients at home;
3) degree of difficulty involved in the administration of the LMWH;
4) acceptance of the prophylaxis (LMWH) by the patients;
5) Colour Echo-Doppler of the superficial and deep venous systems of both lower limbs, and
5) CT (only in cases of clinical suspicion of pulmonary embolism). At 30 days: a) clinical assessment of thromboembolic events (between day 10 and 30), and b) study of morbidity and mortality.

Echo-Doppler

On day 10 after surgery, a colour Echo-Doppler (ED) study was performed to establish the presence of deep or superficial venous thrombosis When there were doubts about the diagnosis in the first

exploration, a second ED was obtained 7 days later. The study was carried our by two expert sonographists, who were blind in the sense that they did not know which risk groups the patients belonged to.

A Toshiba Aplio XG™ with a multisequence linear probe was used. A frequency of 7.5 MHz was employed for the inguinal, thigh, and popliteal zone. Frequencies of 9–10 MHz were used for the great saphenus vein, with variations in both sectors, depending on the body mass index of the patient.

With the patient in the supine position, transverse and longitudinal images of the common femoral, femoral and popliteal veins of the deep venous system and of the great saphenous vein in proximal sectors until the crook of that vein was obtained in mode B in both lower limbs. Compressions were consistently made in all these venous sectors until total collapse of the lumen.

Following this, spectral flow images were obtained in both common femoral veins, placing special emphasis on the morphological aspect of the wave, together with measurements of flow rate in those locations. To obtain the venous spectrum and velocity in both common femoral veins an attempt was made to modify the incidence of the beam until an angle between 30 and 60º was achieved, adjusting the PRF (Pulse Repeat Frequency) to the minimum possible in order to avoid artefacts due to "aliasing". After correcting the angle, a measurement was obtained in the highest region of the curve that corresponded to the expiratory phase when venous return is favoured [6].

With the measurement of venous flow and diameter at the level of the common femoral vein peak blood velocities (cm/sec) and cross-sectional area (cm^2) [7–9] were calculated, which are accepted parameters for the measurement of a pre-thrombotic state characterised by venous stasis [10].

The second echographic assessment, carried out one week after the first one and after continuing treatment with LMWH (in the cases in which it was being administered), was performed when flows of less than 10 cm/s were detected or when flows were below 15 cm/s with alterations associated with the morphology and the spectral trace (mainly the loss of fascicity) or when mobile internal echoes were detected in mode B echography with flows not clearly detectable by the colour Doppler.

Statistical study

Using the Filemaker Pro 8.5 Advanced database, we compiled a data acquisition document in which we included all the data relative to each patient who agreed to participate in the study and signed the written consent form.

The SPSS 15.0 program was employed to perform the statistical calculations of means and standard deviations, the Chi-squared test, Student's t test for the comparison of means with paired groups on comparing the flows in both limbs in a single individual, or independent groups on comparing the flows in one limb of patients with a low, moderate or high risk of VTE. Statistical significance was set at $p<0.05$.

Results

Of the 402 patients included in the study, 357 (88.8%) completed it. Two patients did not comply to the treatment with LMWH, and in the follow-up 43 patients were lost. Finally, 119 (33.3%) (non-risk group/without Bemiparin) and 238 (66.6%) (risk groups/with Bemiparin) were studied; in the latter group, 30 patients (12.6%) were high risk (Fig. 1).

Table 2 shows the surgical and personal risk factors stratifying the patients within a given risk group.

In the Bemiparin groups, we observed high percentages of a) compliance (adherence to the prophylaxis); b) administration by the patients themselves or a family member (i.e. not requiring health-carer attention) and c) acceptance of the method by the patients (Fig. 2).

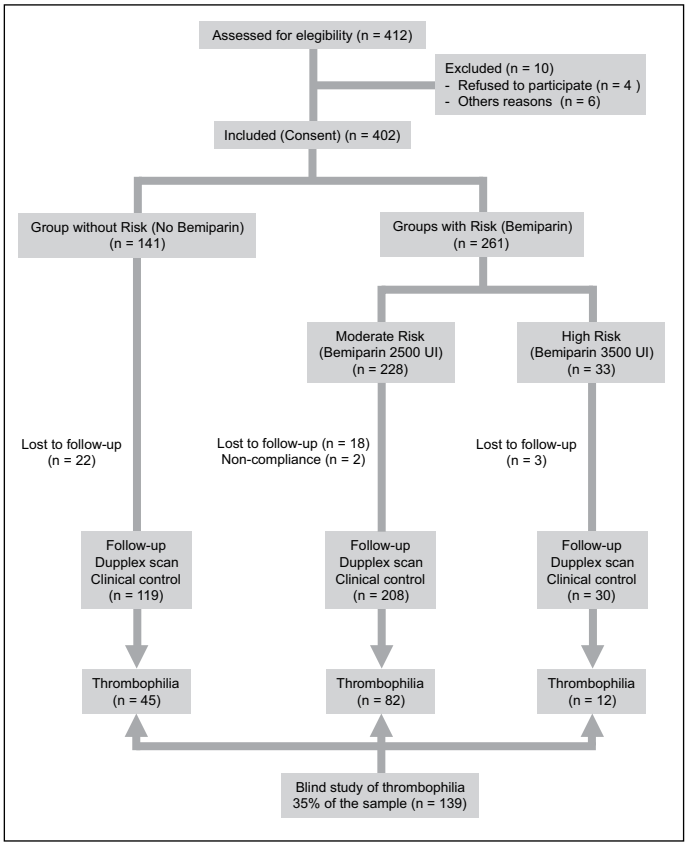

Figure 1 Inclusion, loss, withdrawal and definitive follow-up of patients.

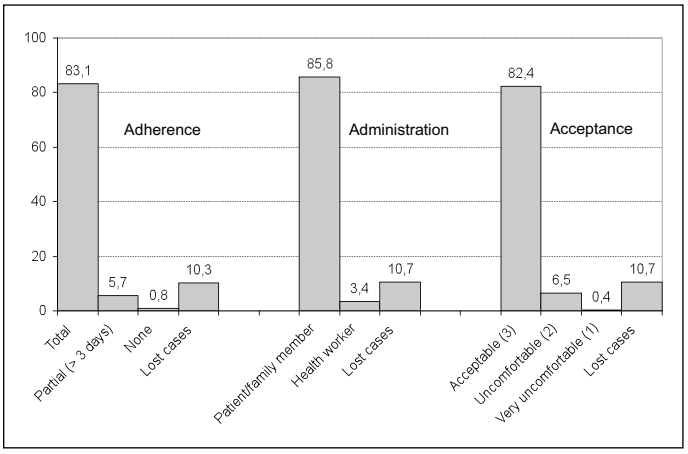

Figure 2 Results (in percentages) of compliance or adherence to prophylaxis, who administered the low molecular weight heparin, and its acceptance by the patient (scale from 1 to 3).

Thromboembolic events

No symptomatic events were observed. We only noted one asymptomatic deep venous thrombosis (femoral vein) in the Bemiparin group (of moderate risk), revealing an incidence of 0.48% (1/208 cases) or 0.28% (1/357) when the whole series was taken into account. No helical TC was performed since no symptoms/signs suggestive of pulmonary embolism were observed during the 30-day follow-up period (Table 3).

Overall, in 39 patients (10.9%) we observed the existence of a decrease in venous flow -lower than 15 cm/sec- in one of the two common femoral veins. This was significantly higher ($p<0.001$) in the risk groups (15.9 and 10%) than in the non-risk group (2.5%). Two weeks after the surgery (according to the second echo-Doppler) all the patients had femoral vein blood flows above 15 cm/s in both lower limbs (Table 4).

Table 2 Risk factors by groups.

	No risk No LMWH N = 14z1	Moderate risk 2500 LMWH N = 228	High risk 3500 LMWH N = 33	Total N =402
Personal factors				
Age (x ± DS)	27.6 ± 7.1	54.5 ± 10.3	54.6 ± 9.6	
< 40 years	141	5*	0	146 (36.3%)
> 40 years	0	223	33	256 (63.7%)
Sex (M/F)	102/39	192/36	33/0	327/75
Type of surgery				
Inguinal hernia:				
Unilateral	59	163	0	222 (55.2%)
Bilateral	0	2	29	31 (7.7%)
Crural hernia	2	14	0	16 (4%)
Umbilical hernia	10	31	0	41 (10.2%)
Epigastric hernia				
Double hernias	0	3	4	7 (1.7%)
SCPSD**	60	4	0	64 (15.9%)
Others	4	4	0	8 (2%)
Type of anaesthesia				
General	47	90	17	154 (38.3%)
Regional	92	135	16	243 (60.5%)
Local /sedation	2	3	0	5 (1.2%)
Length of surgery* **				
< 30 m	141	223	0	364 (90.5%)
> 30 m	0	5	33	38 (9.5%)

* 2 bilateral inguinal hernias, 2 double hernias, 1 previous DVT

** SCPSD = Sacrococcygeal pilonidal sinus disease *** Excluding anaesthesia time

Table 3 Adverse thromboembolic events and haemorrhagic complications by groups.

	No risk No LMWH N = 119 # (%)	Moderate risk 2500 LMWH N = 208 # (%)	High risk 3500 LMWH N = 30	Total N = 357
DVT	0 (0)	1 (0.5)	0 (0)	1 (0.3)
Altered flow (1)	3 (2.5)	33 (15.9)	3 (10)	39 (10.9)
PE	0 (0)	0 (0)	0 (0)	0 (0)
Complications				
Haemorrhage surgical wound*	0 (0)	6 (2.9)	1 (3.3)	7 (2)
Scrotal haematoma**	2 (1.7)	3 (1.4)	1 (3.3)	6 (1.7)
Ecchymosis (2)				
Extensive	-	9 (4.3)	1 (3.3)	10 (4.2)
Minimum***	-	84 (40.4)	12 (40)	96 (40.3)
Allergy (3)		1 (0.5)	0 (0)	1 (0.4)

DVT = Deep vein thrombosis PE = Pulmonary embolism

(1) Venous flow at the level of the common femoral vein < 10–15 cm/s. (2) Site of injection of LMWH

(3) Related to the LMWH

* Did not require transfusion ** No cases required drainage

*** Less than 2 cm in diameter and on only one occasion

The percentage of scrotal haematomas is half of 3.3% if operated inguinal hernias are considered (all were bilateral)

Table 4 Venous flows (measured at the level of the common femoral vein) by groups.

	No risk No LMWH	Moderate risk 2500 LMWH	High risk 3500 LMWH
1st control (N = 39)			
	N = 3	N = 33	N = 3
Pathological flow*	12.32 ± 2.81	10.65 ± 4.12	10.40 ± 3.22
2nd control (N = 39)			
Lower flow**	19.39 ± 9.82	19.39 ± 6.92	17.73 ± 7.46
Higher flow**	22.06 ± 9.29	23.85 ± 21.27	19.96 ± 7.54
1st control (N = 357)			
	N = 119	N = 208	N = 30
Lower control**	28.76 ± 10.88	20.11 ± 7,46	20.10 ± 5.47
Higher flow**	30.35 ± 12.33	21.57 ± 10,36	21.80 ± 9.12

* A flow of < 15 cm/s was measured in at least one common femoral vein ** Taken from one the common femoral veins (left or right)

Haemorrhagic complications

The most frequent complication derived from the administration of LMWH was ecchymosis at the injection site: lowest manifestation 40.3% (<2 cm diameter and on only one occasion) and 4.2% in the more extensive forms. No differences were observed between the two doses of LMWH employed.

The presence of haemorrhage at the surgical wound appeared in 7 patients (2%). Only the patients who received LMWH showed this complication (2.9% and 3.3% in the 2,500 and 3,500 IU Bemiparin groups respectively). The difference was statistically significant ($p<0.001$). None of the haemorrhages was sufficiently important to warrant blood transfusion, although one case required wound drainage and haemostasis.

In contrast, in all three groups the male patients operated on for inguinal hernias developed scrotal haematomas at similar proportions (no Bemiparin and 2,500 and 3,500 IU Bemiparin). None required drainage.

One patient showed intolerance to Bemiparin in the form of cutaneous erythema.

Impact of thrombophilia

Random studies of thrombophilia were conducted in 139 patients (34.6% of the total sample. We found 39 patients (28.1%) with one or more thrombophilic alterations (excluding MTHFR). The most frequent situation, apart from MTHFR (48.6% of the individuals investigated), involved elevated levels of homocysteine (>15 µg/dL) in 12.2% of the patients. The rest (and their division by groups) can be seen in Table 5.

Table 5 Study of thrombophilia by groups.

	No risk No LMWH N = 141	Moderate risk 2500 LMWH N = 228	High risk 3500 LMWH N = 3	Total N = 402
Patients investigated	45/141 (31.9%)	82/228 (36%)	12/33 (36.4%)	139/402 (34.6%)
Patients with thrombophilia*	12/45 (26.7%)	24/82 (29.3%)	3/12 (25.0%)	39/139 (28.1%)
Type of thrombophilia				
AT-III deficit	2	11	2	15 (10.8%)
PC deficit	1	0	0	1 (0.7%)
PS deficit	0	0	0	0 (0)
FV Leiden (+/-)	1	1	0	2 (1.4%)
FV Leiden (+/+)	0	0	0	0 (0)
FII20210 (+/-)	1	2	1	4 (2.9%)
FII20210 (+/+)	0	0	0	0 (0)
R-APC no FVL	3	3	0	6 (4.3%)
Homocysteine	8	9	0	17 (12.2%)
Combinations*	4	2	0	6 (4.3%)
MTHFR (+/-)	20	25	7	52 (37.4%)
MTHFR (+/+)	2	11	0	13 (9.4%)
Total MTHFR	22	36	7	65 (46.8%)

*Excluding methylenetetrahydrofolate reductase (MTHFR) Antithrombin-III deficit (< 80%) Protein C and S deficit (< 60%) Resistance to active protein C (R-APC < 2.5) Hyperhomocysteinaemia > 15 ug/dL **Note:** heterozygote (+/-);homozygote (+/+)

Based on the results on thrombophilia (*a posteriori*), and attending to the consensus that we wished to validate, the patients were transferred from the risk group they had been assigned to *a priori* (without knowing the results on thrombophilia). Thus, the non-risk group decreased when 38 patients were passed to the moderate risk group. Overall, the highest risk increased by 67 when patients from the moderate risk group were transferred to the high risk group (Fig. 3).

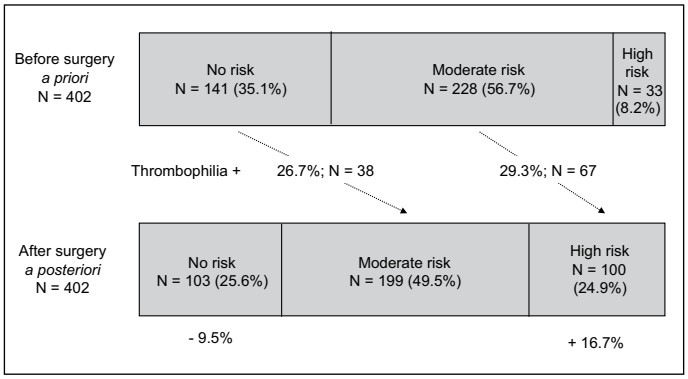

Figure 3 Distribution of the series by risk groups, according to the consensus (Before – *a priori* – and after – *a posteriori* –) knowing the results concerning thrombophilia. It may be seen that the group with no risk decreases while the high-risk group increases.

Discussion

Despite the high frequency and the enormous socio-economic relevance of Major Ambulatory Surgery (MAS), there is a surprisingly small body of information about venous thromboembolism (VTE) in this type of surgery. In fact, only a few consensuses or guides of the many available address the need to identify patients at risk and use thromboprophylaxis in them [3,4]. It should not be overlooked that together with clinical priorities VTE is one of the conditions most frequently involved in medical malpractice suits and the cause of litigation in the United States [11].

The risk of VTE after MAS is not known with precision. Different studies, all of them retrospective [12–15], have reported a low incidence of VTE in patients undergoing MAS. However, four prospective studies that included a systematic screening of VTE (ultrasonography in three, and phlebography in the other) report quite high indices of VTE. Despite this, it is important to note that those studies, included in the excellent review by Ahonen [16] refer only to knee arthroscopy.

It is true that MAS usually involves less invasive surgical techniques and is of shorter duration, implying faster patient recovery. Notwithstanding, it is also the case that patients undergoing MAS are increasingly older, with greater co-morbidity, and that young patients with the risk of VTE must also be addressed [16,17]. Moreover, anaesthetic techniques have been improved and, as seen in our series, regional techniques have gained considerable ground over general anaesthesia. Although the implementation of neuroaxial anaesthesia has a protective effect against VTE [18], this technique, together with the outpatient context of MAS, may hinder or compromise correct application of thromboprophylaxis. In fact, the combination of neuroaxial anaesthesia and antithrombotic drugs makes it necessary to use safety intervals during MAS; these are well known and have been perfectly established in the medical setting [19].

Although based on retrospective studies, a low incidence of VTE has been reported for surgery of inguinal hernias and other interventions in the abdominal wall [12,14]. However, since hernia surgery is one of the most frequent surgical procedures [20] there must necessarily be patients at risk of VTE. It is well known that effects (benefits/risks) and costs are maximally optimized when patients are well stratified.

Just as there is little information about the risk of VTE in MAS, there are also very few studies investigating thromboprophylaxis in MAS, especially if they do not address orthopaedic or laparoscopic surgery [1,4,16,21–24]. Thus, in the meta-analysis carried out by Mismeti et al [25] on low-molecular weigh heparins (LMWH) in the prophylaxis of VTE in general surgery, none of the 59 clinical trials selected by those authors involved MAS. The same is the case of a later review on LMWH in the prevention of VTE after abdominal surgery [26].

Indeed, we are unaware of any randomized and controlled clinical trial that reports the value of thromboprophylaxis in MAS (hernias, proctology, etc). As far as we know, there are only three non-randomised studies: the first involved a short series of 114 patients undergoing inguinal hernia repair [27] who were treated with calcium heparin at low doses, but with the aim of assessing the influence of the injection site on the appearance of complications at the level of the post-operative wound. The second one was a retrospective study [14] in 1854 patients operated for hernias who received prophylactic heparin, although the authors did not refer to the reason for its indication (risk stratification) or the methodology used (type, dose, initiation and duration). The last one was a non-randomised observational prospective study [28] in which Bemiparin (LMWH) was used prophylactically in 203 patients undergoing open or laparoscopic abdominal wall surgery (hernias and eviscerations) with moderate (81.1%) or high (26.1%) risk factors according to the THRIFT Consensus Group from 1992. However, the greatest problem with this study is that no systematic screening of deep vein thrombosis (DVT) was performed.

Despite the poor reliability of the few data available, there is concern about the need for thromboprophylaxis in this type of patient, as demonstrated by the existence of many questionnaires addressing the issue [17,24,29–31]. According to the opinions of the surgeons involved in them, who were from different European and North American countries, the issue should remain under debate since some studies involved stratified risks, while some did not; in some, thromboprophylaxis was implemented, while in others it was not. What is certain is that the numbers and complexity of MAS are increasing and hence it is not surprising that many such questionnaires conclude by requesting the creation of some kind of consensus as regards the actions to be taken.

Many scientific societies and panels of experts have proposed recommendations concerning the prevention of VTE in surgical patients. However, there are very few specific recommendations for MAS. This has led to uncertainty and variability in the guidelines for action. A consensus in this regard was reached in 2006 by the Spanish ASECMA group [5].

Our prospective study, mainly related to abdominal wall surgery, has allowed us to validate the above mentioned consensus concerning thromboprophylaxis with LMWH in MAS. Our observations support the hypothesis that one group of MAS patients was at low risk and did not require thromboprophylaxis with LMWH. This first group formed more than one third of the series (141/402). Since prophylaxis with LMWH is not free of risks in MAS, mainly in the form of haemorrhage (22,28,32), this group benefited additionally from the non-implementation of a systematic policy of prophylaxis in MAS.

Complementary to the stratification of VTE, we were surprised to find that nearly two-thirds of the patients were at moderate or high risk. In them, as in other studies (33), Bemiparin – a second generation LMWH – at doses of 2,500 and 3,500 IU/day, depending on the individual risk, proved to be effective in preventing VTE. Additionally, it proved to be effective when administered in the post-operative period, the risk of haemorrhage (including the injection site) being very low, as reported previously [34].

Logically, since there are few data available about the indication for LMWHs in MAS, there are even fewer data concerning the way such compounds are used. According to the review of Ahonen [16], the optimum time for initiating thromboprophylaxis in MAS is 6 h after surgery. Since there is no evidence to support single dose or 1–2 days of thromboprophylaxis, we chose the protocol indicated in most studies, which extends administration to 7–10 days or until the patient feels confident about walking normally [1,2)].

One of the major limitations of our study is the assessment of the results. As reported by Geerts et al [1], trials should measure efficacy and innocuousness together as the optimum result. Owing to the strong concordance between asymptomatic DVT and VTE, DVT must be investigated through the use of sensitive detection tests such as phlebography. However, although phlebography is sensitive for the detection of DVT, it is invasive, regardless of whether 20-40% of the venograms are considered non-diagnostic, and the clinical outcome of small thrombi seems uncertain. In contrast, apart from its low cost colour Echo-Doppler (ED) is a well known method for the diagnosis of DVT [35], is widely available, is non-invasive (non-iatrogenic) and is repeatable. However, the accuracy of ED is reduced in the case of the calf veins, is operator dependent, and the assessment of ED in clinical trials is difficult [36]. The sensitivity of ED in the follow-up of asymptomatic patients in the post-operative period has been questioned [37].

Aware that each method has its strengths and weaknesses, we thought it excessive to request a bilateral phlebography for the asymptomatic ambulatory patients. Accordingly, it is strange that many trials, mainly in laparoscopic surgery, have used ED [7–10,37,38]. With a serial bilateral ED (where necessary), results such as symptomatic VTE (or the combination of asymptomatic VTE and asymptomatic proximal DVT) can be objectified, together with the most important results on safety. In fact, the combination of venous compressibility and a study of spectral flow are the elements that provide the best sensitivity and specificity as regards the detection by ED of probable thrombotic problems in the venous system of limbs.

Normal venous flow is characterised by the absence of echoes or by a discrete intralumen echogenicity and a continuous flow inside the vein. The typical aspect of the spectral wave in the lower limbs is that of a spontaneous, phase-like anterograde flow, the fascicity being governed by the movements of inspiration-expiration under normal conditions. If cardiac alterations are present, the pressure in the right auricle will also lead to changes in the shape of the wave. It is also known that flow velocities in the arterial system are fairly constant in the different territories of the body, which is not the case of venous velocities, which are subject to many factors such as respiratory movements, the cardiac cycle, blood volume, valve competency, and even the body mass index, among others. In our series, although there was considerable variability in venous flow velocity, as mentioned previously, we performed a second assessment one week after the first one and after recommending continuation of the treatment with LMWH (in cases in which it was being administered) when we detected flows of les than 10–15 cm/s. All patients had improved their velocities by the second exploration.

In light of our results, it may be concluded that in MAS there are different groups at risk of VTE. The low risk patients only require the usual preventive measures (e.g., early and maintained walking) and do not need LMWH, thus being free of possible risks attributable to the drug. Nevertheless, there are larger groups with risk factors. To confirm whether these groups are at risk, might it be right to perform a randomised controlled study with a placebo in such individuals?. Clearly, with the results it would be possible to determine whether these groups, which we have called moderate and high risk (as a function of the stratification carried out), require LMWH at the above described doses over time. In view of the results on efficacy and safety, we would not feel confident about taking such a step, especially since we observed an important number of situations of venous stasis and hidden thrombophilia, both of which are able to further exacerbate risk. Another possibility would be to modify some aspect of the methodology used for the administration of LMWH. It would seem that initiation at 6 h after anaesthesia (especially in the case of neuroaxial anaesthesia) would be an ideal moment to start pharmacological thromboprophylaxis, since it does not modify efficacy and increases safety. However, in view of the ambulatory nature of this type of patient, it might be more interesting to reduce the administration of the drug to 1–2 days, which – without changing effectiveness – could improve the safety parameters and overall costs.

In summary, MAS is not free of VTE events. The risks of this kind of patient need to be stratified in order for the pertinent decisions to be taken. Patients considered to be at moderate/high risk of VTE benefit from post-operative administration of Bemiparin, with a low risk of -mostly minor- complications. This prophylactic practice is effective and safe and is accepted by most patients who demand of MAS the maximum quality in medical attention.

Addendum: the role of each author

Francisco S. Lozano: conception and design of the study, data acquisition, analysis and interpretation of the data, manuscript drafting and administrative support.

José Sanchez-Fernandez: data acquisition and interpretation (study surgeon), statistical analysis, and critical review of the manuscript.

José A. Santos and Jesús García-Alovio: data acquisition and interpretation (study echographists), critical review of the manuscript.

Rafael Mateos: data acquisition and interpretation (study surgeon) and critical review of the manuscript.

José R. González-Porras and Ignacio Alberca: data acquisition and interpretation (study of thrombophilia), critical review of the manuscript.

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