Suitability of the Use of Low-Molecular-Weight Heparins in the Prevention of Venous Thromboembolism

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Abstract

Objective: To investigate the prevalence of low-molecular-weight heparins (LMWH) prescription in venous thromboembolism prophylaxis in a general hospital and the suitability of the recommendations from the clinical practice guidelines.

Method: A descriptive, observational, and cross-sectional study of the indication-prescription type, carried out on patients admitted to medical departments and for surgery.

Results: Three hundred forty-five patients were included. The prevalence of LMWH use was 44.6% (95% CI, 39.3-50.1). Depending on the risk of thromboembolism, the decision to treat prophylactically (or not) was appropriate in 261 cases (75.7%; 95% CI, 70.7-80.1), and the action guidelines were not suitable for the remainder of patients. Fifty-five patients (15.9%; 95% CI, 12.2-20.2) presented a high risk and were not prescribed prophylactically (underuse); and 29 patients (8.4%; 95% CI, 5.7-11.8) at low risk were treated prophylactically (overuse). There was a relationship between the appropriateness of the prescription and the type of patient ($P<.01$). In the group of medical patients the prevalence of prescription was 22.6% (95% CI, 16.9-29.1) and only 33.3% of patients with a high to moderate risk of thromboembolism received prophylaxis. The prevalence of prescription in general surgery was 84.2% and 91.3% in traumatology.

Conclusions: The degree of prophylaxis is adequate in surgical patients, but there was a significant percentage of medical patients with a high to moderate risk who did not receive suitable prophylaxis (underuse), despite recommendations with scientific and professional backing.

Key words: Prevalence. Cross-sectional studies. Drug utilization review. Venous thromboembolism. Prophylaxis. Low-molecular-weight heparins.

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Adecuación de la utilización de heparinas de bajo peso molecular en la prevención de la enfermedad tromboembólica venosa

Objetivo: Conocer la prevalencia de prescripción de heparinas de bajo peso molecular (HBPM) en la profilaxis de la enfermedad tromboembólica venosa en un hospital general, así como la adecuación a las recomendaciones de las guías de práctica clínica.

Método: Estudio observacional, descriptivo, de corte transversal, tipo indicación-prescripción, con pacientes ingresados en servicios médicos y quirúrgicos.

Resultados: Se incluyeron 345 pacientes. La prevalencia de prescripción de HBPM fue del 44,6% (intervalo de confianza [IC] del 95%, 39,3-50,1). Según el nivel de riesgo tromboembólico se encontró adecuación en la decisión de tratar profilácticamente (o no) en 261 casos (75,7%; IC del 95%, 70,7-80,1), en el resto la pauta de actuación no fue la adecuada, destacando 55 pacientes (15,9%; IC del 95%, 12,2-20,2) con riesgo alto a los que no se había prescrito profilaxis (infrautilización), y 29 pacientes (8,4%; IC del 95%, 5,7-11,8) con riesgo bajo que estaban con profilaxis (sobreutilización).

En los pacientes médicos la prevalencia de prescripción fue de 22,6% (IC del 95%, 16,9-29,1) y sólo el 33,3% de los de riesgo tomboembólico alto-moderado recibió profilaxis. La prevalencia de prescripción en cirugía general fue del 84,2% y en traumatología del 91,3%.

Conclusiones: En pacientes quirúrgicos el nivel de profilaxis alcanzado es adecuado, pero hay un porcentaje importante de pacientes médicos con riesgo tromboembólico medio-alto, que sigue sin recibir la adecuada profilaxis (infrautilización), a pesar de las recomendaciones de consenso con amplio respaldo científico y profesional.

Palabras clave: Prevalencia. Corte transversal. Estudio de utilización de medicamentos. Enfermedad tromboembólica venosa. Profilaxis. Heparinas de bajo peso molecular.

INTRODUCTION

Venous thromboembolism (VTE) is an ongoing issue. The health significance of this disease lies in the morbidity and mortality of pulmonary thromboembolism (PTE) and post-thrombotic syndrome, principal complications of deep venous thrombosis (DVT). According to recent population studies, annual incidence of DVT is 50 per 100 000 persons and 70 per 100 000 for PTE. However, actual incidence of the problem could be greater because the majority of VTE is asymptomatic.[1] In the United States, there are 150 000-200 000 deaths annually from VTE, and despite treatment advances, 1 of 10 hospital deaths are due to PTE, 75% of these occurring in non-surgical patients.[2] In Spain, PTE is the third cause of death among cardiovascular diseases, behind ischemic cardiopathy and ictus.[3] Furthermore, it represents the first cause of preventable inpatient death.[3] The high incidence of VTE combined with its serious consequences makes the correct prophylaxis for medical and surgical patients a priority objective for the health system. In spite of strong evidence on the effectiveness of prophylactic treatments, there is broad variation in the application of these methods in clinical practice.[4,5] Various surveys find fluctuations from 28% to 100% in regular use of this prophylaxis.[4] Low-molecular-weight heparins (LMWH) are the main drug choice for treatment, and in fact, in recent years, various practice guidelines have been published on VTE prophylaxis which recommend LMWH drug prophylaxis as a main method of prevention.[2,4-9]

In view of these facts, finding if LMWH is used effectively and rationally in VTE prophylaxis is an issue of great interest. Because of this, this study was established, with a principal objective of finding the prevalence of LMWH prescription for VTE prophylaxis in a general hospital and the suitability of the recommendations of clinical practice guidelines.

METHOD

An observational, descriptive, and cross-sectional study (30/11/05), of the indication-prescription type, carried out in Hospital Juan Ramón Jiménez of Huelva (hospital with specializations, 553 beds and medical residency).

Inclusion criteria: patients admitted to the departments of internal medicine, pneumology, neurology, digestion, cardiology, oncology, haematology, nephrology (excluding haemodialysis), general surgery, gynaecology, vascular surgery, traumatology, urology, otolaryngology, ophthalmology, neurosurgery, and multipurpose intensive care unit (ICU). These departments cover 77% (425) of the hospital's beds.

Exclusion criteria: patients in thromboembolism treatment (received non-fractionated heparin [NFH] or LMWH at therapeutic dosages at the time of the cross-sectional) or anticoagulants (received acenocoumarol or warfarin) at the time of the study.

The main variable was the prevalence of LMWH prescription for thromboembolism prophylaxis, and other demographic and clinical characteristics were collected (Appendix 1).

To evaluate adequacy of LMWH treatment, 2 variables were taken into account: thromboembolic risk and dosage used.

Thromboembolic risk was measured as a categorical variable and classified as *"low," "moderate,"* or *"high"* according to risk factors present and taking into account specific epigraphs from the 7th Consensus Conference of the American College of Chest Physicians (ACCP)[5] for surgical patients, and the PRETEMED guidelines[6] for medical patients.

The LMWH dosage used was classified as *"no LMWH"* (patient with no dosage of LMWH), *"low dosage"* (20 mg of enoxaparin, the LMWH is enoxaparin, which is the only drug included in the drug treatment guidelines of Hospital Juan Ramón Jiménez), *"high dosage"* (40 mg of enoxaparin).

According to the aforementioned recommendations, patients with a "high" thromboembolic risk should receive a "high" dosage of LMWH; those with "moderate" thromboembolic risk receive a "low" LMWH dosage, and those with a "low" thromboembolic risk should not receive LMWH prophylaxis[2,4-9] (Appendix 2). These risk and dosage combinations could be defined as "suitable." A synthetic variable was established to evaluate the suitability of LMWH prescription for thromboembolic risk with 3 categories: underuse (patients with moderate or high thromboembolic risk who had any contraindication to LMWH use and were not prescribed this were classified in the underuse group), overuse, and suitable use (Table 1).

Likewise, for the purpose of evaluating the dosage correction used, another synthetic variable was established called suitability of dosage for thromboembolic risk, also with 3 distinct categories: suitable guideline, underdosage, and overdosage (Table 1).

Five forms for data collection were designed (general surgery, traumatology, and orthopaedic surgery, other surgeries, medical patients, and ICU patients) which were previously subject to a pilot study.

The calculation of the sample's size was carried out by the program Epiinfo version 6, taking the following parameters: prevalence of LMWH prescription for thromboembolism prophylaxis of at least 32% (according to published data from other previous descriptive studies[10-12]), precision for detecting

Table 1. Suitability of the Prescription and Dosage for Thromboembolic Risk

		Dosage LMWH		
		No LMWH	Low	High
Thromboembolic Risk	Low	Suitable use (suitable guideline)	Overuse	Overuse
	Moderate	Underuse	Suitable use (suitable guideline)	Suitable use (overdosage)
	High	Underuse	Suitable use (underdosage)	Suitable use (suitable guideline)

LMWH: low-molecular-weight heparin.
Underuse: patients with high or moderate thromboembolic risk, not prescribed LMWH.
Overuse: patients with low thromboembolic risk, prescribed LMWH.
Suitable use: patients with moderate or high thromboembolic risk, prescribed LMWH, and patients with low thromboembolic risk, not prescribed LMWH.
Suitable guideline: patients with high or moderate thromboembolic risk, prescribed a high or standard dosage of LMWH, respectively, and patients with low thromboembolic risk, not prescribed LMWH.
Underdosage: patients with high thromboembolic risk, prescribed a standard dosage of LMWH.
Overdosage: patients with moderate thromboembolic risk, prescribed a high dosage of LMWH.

differences of at least 5% around actual prevalence, and a 95% confidence level (alpha error of 5%). These parameters required a sample size of 335 patients.

The statistical analysis was carried out by the SPSS-Windows version 12.0 software package. Descriptive statistics were carried out for all of the study's variables, as a whole, and by patient type. A multiple logistic regression was carried out for determining variables associated with LMWH use.

RESULTS

The day when the cross-sectional was carried out, there were 404 inpatients in the departments involved in the study. Fifty-nine were excluded because of aforementioned reasons. Of all patients, 154 received LMWH prophylaxis, and this was a prescription prevalence of 44.6% (95% confidence interval [CI], 39.3-50.1). Of all prescriptions, 33.8% were for medical patients and 66.2% for surgical patients. General characteristics of the study's population are shown in Table 2.

The assessment of thromboembolic risk and dosages used are shown in Table 3. The χ^2 test used for the comparison of thromboembolic risk variables and the type of dosage used showed an association between them ($P<.01$).

Analyzing only high-moderate thromboembolic risk patients comprising 52.2% of the sample, 69.4% received prophylaxis; in the rest, underuse was detected. Analyzing only low thromboembolic risk patients—those who should not receive prophylaxis—, 82.4% did not receive it; overuse was detected in the rest (Figure 1).

Table 2. General Characteristics

Characteristic	No. (%)	95% CI
Age	61.7[a]	59.9-63.5
Sex		
Males	212 (61.4)	56.1-66.6
Females	133 (38.6)	33.4-43.9
Medical patients[b]	205 (59.4)	54.0-64.6
Cardiology	7 (3.4)	
Vascular surgery	3 (1.5)	
Digestion	16 (7.8)	
Gynaecology	2 (1)	
Haematology	14 (6.8)	
Internal medicine	72 (35.1)	
Nephrology	16 (7.8)	
Pneumology	19 (9.3)	
Neurology	23 (11.2)	
Oncology	12 (5.9)	
Otolaryngology	3 (1.5)	
Traumatology	1 (0.5)	
ICU	10 (4.9)	
Urology	7 (3.4)	
Surgical patients	140 (40.6)	35.4-46.0
General surgery	37 (26.4)	
Vascular surgery	7 (5)	
Gynaecology	13 (9.3)	
Nephrology[c]	1 (0.7)	
Neurosurgery	2 (1.4)	
Ophthalmology	3 (2.1)	
Otolaryngology	15 (10.7)	
Traumatology	46 (32.9)	
Urology	16 (11.4)	

CI indicates confidence interval; ICU, intensive care unit.
[a]Average age.
[b]Patients admitted for surgery due to medical pathology and ICU patients were included, but ICU patients were analyzed separately.
[c]An operated medical patient was included.

Thromboembolic risk factors of patients with suitable prescriptions were analyzed, and an association was found with the presence of neoplasia and serious acute infection ($P<.01$, in both cases). Likewise, of the 29 overuse patients, 75.9% were over 60 years of age, and in isolated cases, additional risk factors were detected.

Lastly, an association was found between prescription suitability variables and dosage of the type of patient ($P<.01$). Higher adequate use was detected in surgical patients than in medical patients. Underdosage was more common in surgical patients, and underuse and overuse in medical patients.

Table 3. Distribution of Patients Depending on Dosage Used and Thromboembolic Risk

	Dosage Used			
Thromboembolic Risk	**No LMWH**	**Low Dosage**	**High Dosage**	**Total**
Low (% risk)	136 (82.4)	3 (1.8)[b]	26 (15.8)[b]	165 (100)
Moderate (% risk)	18 (41.9)[a]	16 (37.2)	9 (20.9)	43 (100)
High (% risk)	37 (27)[a]	12 (8.8)	88 (64.2)	137 (100)
Total (% risk)	191 (55.4)	31 (9)	123 (35.7)	345 (100)

LMWH indicates low-molecular-weight heparin.
[a]Underuse: 55 (15.9%) (95% confidence interval [CI], 12.2-20.2). Of which 29 had contraindications or precaution with LMWH use: 11 (severe thrombopenia), 4 (recent non-active hemorrhage), 14 (serum creatinine ≥1.5 mg/dL).
[b]Overuse: 29 (8.4%) (95% CI, 5.7-11.8).
Without superscript: 261 (75.7%) (95% CI, 70.7-80.1).
- Suitable guideline: 240 (69.6%)
- Underdosage: 12 (3.5%)
- Overdosage: 9 (2.6%)

Medical Patients

A total of 195 patients were hospitalized for medical services (ICU patients were not included), with an average age of 62.75 years, and of these, 63.6% were males. The most prevalent VTE risk factors were, patients over 60 years (61%), obesity (23.1%), and existence of neoplasia (22.6%), or a serious acute infection (22.1%). Fifty-three point three percent presented with 2 or more risk factors simultaneously. Twenty-two point six percent (95% CI, 16.9-29.1) received LMWH prophylaxis, and in the multivariant analysis an association of having prophylaxis and age over 60 years was found (odds ratio [OR], 2.3), bedridden for more than 4 days (OR, 10.9), and having worsened COPD (OR, 5.4).

The assessment of thromboembolic risk and dosages used are shown in Table 4. Analyzing only high-moderate thromboembolic

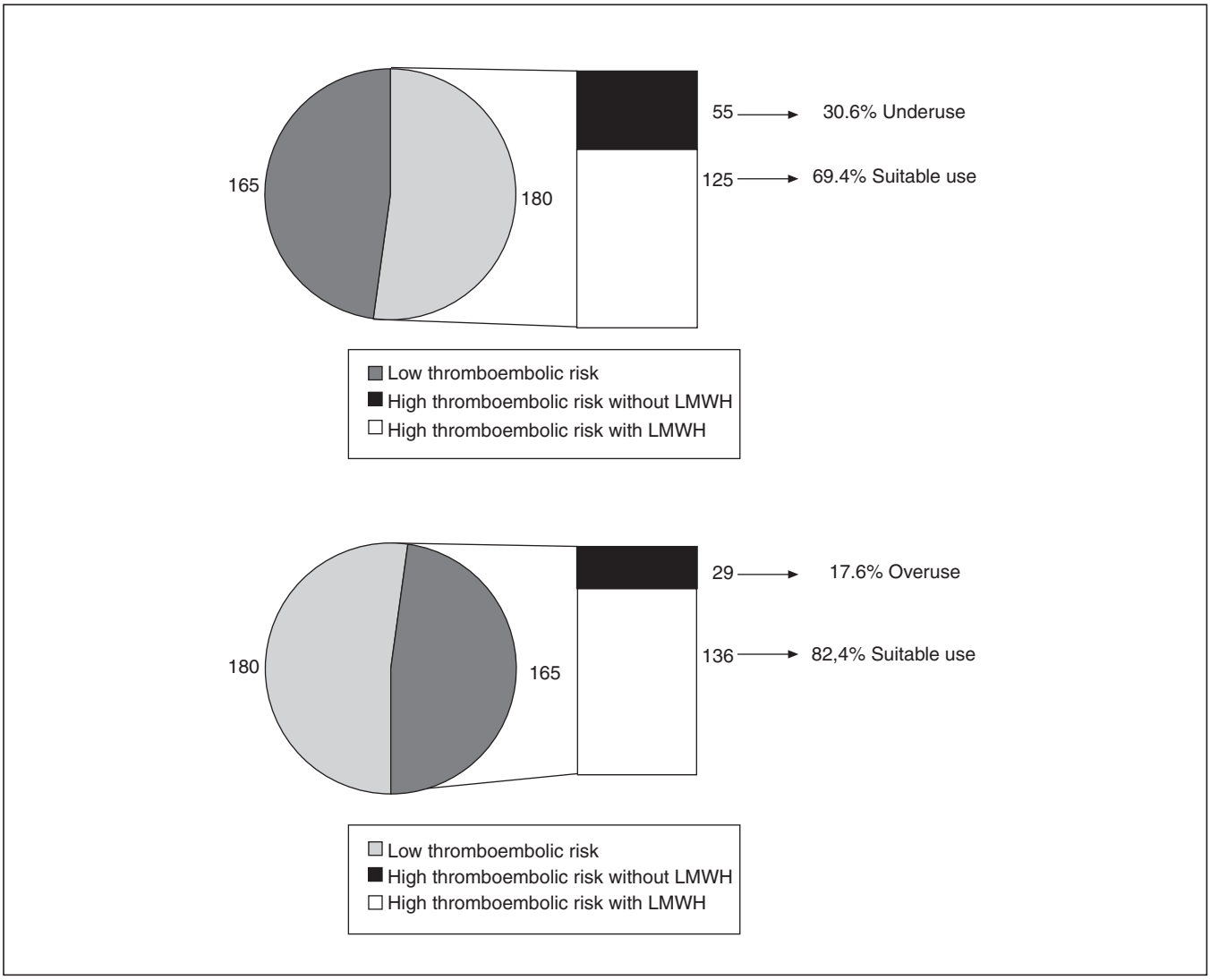

Figure 1. *Analysis of patients with high-moderate thromboembolic risk and those with low thromboembolic risk.*

Table 4. Distribution of Medical Patients Depending on Dosage Used and Thromboembolic Risk

	Dosage Used			
Thromboembolic Risk	**No LMWH**	**Low Dosage**	**High Dosage**	**Total**
Low (% risk)	111 (82.2)	0 (0)[b]	24 (17.8)[b]	135 (100)
Moderate (% risk)	10 (55.6)[a]	2 (11.1)	6 (33.3)	18 (100)
High (% risk)	30 (71.4)[a]	2 (4.8)	10 (23.8)	42 (100)
Total (% risk)	151 (77.4)	4 (2.1)	40 (20.5)	195 (100)

[a]Underuse: 40 (20,5%) (95% confidence interval, 15.1-26.9).
[b]Overuse: 24 (12.3%) (95% CI, 8.1-17.8).
Without superscript: 131 (67.2%) (95% CI, 60.1-73.7).
– Suitable guideline: 123 (63.1%)
– Underdosage: 2 (1.0%)
– Overdosage: 6 (3.1%)

risk patients, only 33.3% received prophylaxis, and underuse was detected in the rest.

Analyzing only low thromboembolic risk patients—those who should not receive prophylaxis—, 82.2% did not receive it, and overuse was detected in the rest (Figure 2).

Surgical Patients

General Surgery

In Table 5, general characteristics of 38 patients from general surgery are shown. Of these, 32 (84.2%) received LMWH thromboembolic prophylaxis.

Depending on risk level, suitability was based on the decision to treat prophylactically (or not) 33 patients (suitable guideline 21, underdosage 10, and overdosage 2), while in 5 patients underuse was detected.

Traumatology

In Table 6, general characteristics of 46 patients from traumatology are shown. Of these, 42 (91.3%) received LMWH thromboembolic prophylaxis. No cases of underuse, underdosage, or overdosage were detected, and there was only 1 case of overuse.

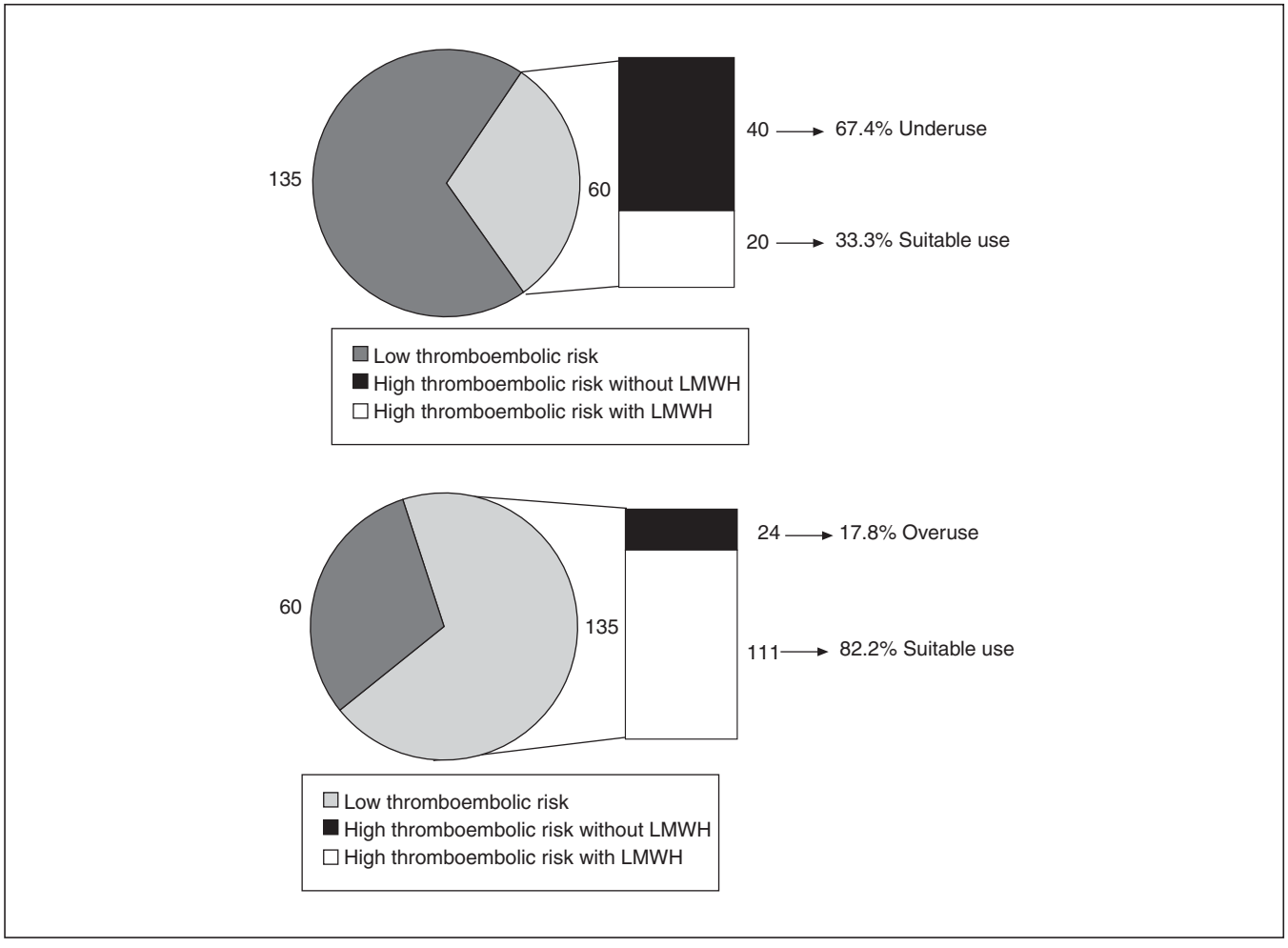

Figure 2. *Analysis of medical patients with high-moderate thromboembolic risk and those with low thromboembolic risk.*

Table 5. Patients From General Surgery

Characteristic	No. (%)	95% CI
Sex		
Males	24 (63.2)	46.0-78.2
Females	14 (36.8)	21.8-54.0
Age, y		
Average	60.7	(55.3-66.0)
<40	3	
40-60	14	
>60	21	
Type of surgery		
Major	25 (65.8)	48.6-80.4
Minor	13 (34.2)	19.6-50.2
Major procedures		
Cholecystectomy	8	
Colon resection	5	
Herniorrhaphy	4	
Gastrectomy	4	
Mastectomy	3	
Thyroidectomy	1	
Duration of intervention (average duration in minutes)	94.4	(72.3-116.5)
Type of anaesthesia		
Single epidural	16	
General	20	
Local	1	
Continuous epidural	1	
Additional risk factors[a]		
0	18	
1	10	
>1	10	
Obesity (BMI >28)	10	
Neoplasia	10	
Serious acute infection	1	
CRF-nephrotic syndrome	3	
Bedridden >4 days	3	
Central venous catheter	4	
Chemotherapy	1	
Smoking (>30 cigarettes/day)	3	
Decompensated COPD	2	
CCF	1	

BMI indicates body mass index; CCF, congestive cardiac failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure.
[a]Age was not included.

Other Surgeries

The remaining surgical patients were grouped in Table 7 because of their smaller representation in the sample. Prophylaxis has been mainly used in urology and gynaecology operations.

ICU Patients

In Table 8, general characteristics of 10 ICU patients are shown. All had to have received prophylaxis with a LMWH high dosage, but this was not used in 2 due to the appearance of a severe thrombopenia which contraindicated the prophylaxis. No patient received any other thromboembolic prophylaxis dosage.

DISCUSSION

The prevalence of LMWH prescription as a prophylaxis for VTE estimated in this study (44.6%; 95% CI, 39.3-50.1) is greater than other publications.

Table 6. Patients From Traumatology

Characteristic	No. (%)	95% CI
Sex		
Males	25 (54.3)	39.0-69.1
Females	21 (45.7)	30.9-61.0
Type of surgery		
Knee arthroplasty	23	
Hip	12	
Tibia	3	
Upper extremities	3	
Femur	2	
Knee arthroscopy	1	
Multiple trauma[a]	1	
Ligament lesions	1	
Duration of intervention (average duration in minutes)	97.8	84.1-111.6
Age, y		
Average	59.9	54.0-65.8
<40	9	
≥40	37	
Type of anaesthesia		
Single regional dose	41	
General	4	
Additional risk factors[b]		
0	41	
1	5	
Obesity (BMI >28)	1	
Neoplasia	1	
Serious acute infection	1	
Previous VTE	1	
Bedridden >4 days	1	
Drugs[c]	1	
Smoking (>30 cigarettes/day)	1	
Decompensated COPD	1	

BMI indicates body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; VTE, venous thromboembolism.
[a]Not intervened.
[b]Does not include age.
[c]Tamoxifen, raloxifene, hormonal replacement therapy, or oral contraceptives.

In a cross-sectional study carried out in 7 Spanish hospitals by the group for the study of thromboembolism of the Spanish Society of Clinical Pharmacology, 32% of patients admitted to internal medicine and general surgery departments received prophylactic treatment with NFH or LMWH.[10]

In another cross-sectional study carried out in the Hospital Juan Ramón Jiménez of Huelva in 2000, in the same departments as this study, 25% of medical and surgical patients received LMWH prophylaxis and 36% received prophylaxis or LMWH treatment.[11] Even though patients in thromboembolic treatment were not excluded at that time, the prevalence of prescription increased notably.

Table 7. Patients From Other Surgeries

Characteristic	No. (%)	95% CI
Age	60.6	56.0-65.2
Sex		
Males	32 (57.1)	43.2-70.3
Females	24 (42.9)	29.7-56.8
Urology	*16*	
≥2 Risk factors	9	
Single epidural anaesthesia	13	
Type of surgery		
Open	9	
Transurethral or less	7	
Duration of surgery (average duration in minutes)	101.5	(62.9-140.2)
Duration of prophylaxis (average duration in days)	10.5	(3.3-17.8)
Gynaecology	13	
≥1 Risk factor	6	
Single epidural anaesthesia	7	
Type of surgery		
Major malignant	2	
Major benign	5	
Others	6	
Duration of prophylaxis (average duration in minutes)	106.7	(74.8-138.5)
Duration of surgery (average duration in days)	7	(2.9-11.1)
Vascular surgery	7	
>2 risk factors	7	
Single epidural anaesthesia	4	
Duration of surgery (average duration in minutes)	76	(38.4-113.6)
Duration of prophylaxis (average duration in days)	17.8	(1.3-34.3)
Otolaryngology	15	
Ophthalmology	3	
Neurosurgery	2	

CI indicates confidence interval.

Table 8. Patients From the Intensive Care Unit (ICU)

Characteristic	No.
Age,[a] y	59.5 (49.1-70.0)
Sex	
Males	7
Females	3
Type of patient	
Medical	8
Multiple trauma	2
Reason for ICU admission	
Respiratory failure	4
Neurological failure	2
Septic shock	2
Serious trauma	2
ICU methods	
Mechanical ventilation	5
Sedative drugs	5
Muscle relaxant	0
Vasoactive drugs	4
Additional risk factors	
2	1
3	4
4	2
5-7	3
Duration of prophylaxis,[a] d	25.6 (11.3-40.0)

[a]Average and 95% confidence interval.

There are various French studies which analyze the prevalence of LMWH prescription for thromboembolism prophylaxis. In a cross-sectional study carried out in 1998 in the Centre Hospitalier Intercommunal de Créteil (France), 36% of medical and surgical patients admitted received prophylactic treatment with heparin.[12] In a therapeutic audit carried out in the Centre Hospitalier de Meaux (France) in the same year, 21% of patients admitted received heparin prophylaxis in a first cross-sectional study, and 23% in a second cross-sectional, carried out after a thromboembolic prophylaxis guideline was put into place.[13]

In another observational cross-sectional study carried out in 2006 by Deheinzelin et al[14] in 4 Brazilian hospitals, prevalence of thromboembolic prophylaxis prescription was 39%.

The main limitations of using previous studies for establishing comparisons are that they came from clinical practice in different countries or were carried out a long time ago, and development of thromboembolic prophylaxis over the last 10 years would itself justify differences.

In medical patients from our study, prevalence of LMWH prescription was detected at 22.6%, but according to the risk assessment carried out, it should be 30.8%. These differences coincide with those found in other studies.

In 2002, the College of Internal Medicine of Paris published results from a cross-sectional study done in 29 French hospitals,

where 32% of hospitalized medical patients received LMWH prophylaxis. Although the level of thromboprophylaxis administered in the study was high, its authors estimated that thromboprophylaxis was necessary in 40% of medical patients.[15]

Likewise, in another cross-sectional study carried out in 2005 by Chopard et al[16] in 8 Swiss hospitals, 49% of patients received prophylaxis, although prescription prevalence according to the study's suitability criteria should have been 59%.

In our study, only 33.3% of high risk medical patients received LMWH thromboprophylaxis and 55% in the study by Chopard et al.[11] Our results coincide with other studies where only one third of high risk thromboembolic medical patients received heparin prophylaxis.[17-20]

In reference to surgical prophylaxis, the prevalence of prescription detected (84.2%) improves that obtained in the study of the Spanish Society of Clinical Pharmacology, where only 53% of patients operated in major surgery received heparin prophylaxis.[10] It is also higher than the study done by Bratzler et al[21] in 1995, in an Oklahoma hospital, where only 38% of patients subject to thoracoabdominal surgery received drug prophylaxis.

In traumatology, the level of LMWH prophylaxis prescription was suitable. Drug prophylaxis should be used in almost all patients admitted for this type of surgery, and only those subject to surgical procedure of the upper extremities, arthroscopy, or lesions of ligaments and soft parts in patients without risk factors are excluded.[5,22,23]

Regarding prescription suitability, patients with high or moderate thromboembolic risk who were not prescribed LMWH make up 30.6%. This level of underuse is not excessively high compared to that found by the study from the Spanish Society of Clinical Pharmacology (*Sociedad Española de Farmacología Clínica*), where 52% of patients with similar characteristics did not receive prophylaxis.[10] This also does not correspond to the data published in the 6th Consensus Conference on antithrombotic and thrombotic therapy of the ACCP, where there are high risk thromboembolic prophylaxis prescription figures of only 39%, or 38% for surgical patients.[4] This is closer to results from the Deheinzelin et al study where, according to the guideline used to measure thromboembolic risk, underuse was at 37 (ACCP guidelines) or at 29% (International Union of Angiology Consensus Statement).[14]

In our study, underuse mainly affected medical patients, and although some had contraindications to LMWH use, at times there were patients with neoplastic or infectious conditions which hold greater thromboembolic risk.

In general surgery, a few cases of underuse were detected despite results of prophylaxis use being acceptable. In view of this, it is important to remember that only patients under 40 without additional risk factors who will be subject to minor surgery, may do without LMWH thromboembolic prophylaxis.[2,5]

Overuse affected 17.6% of patients prescribed LMWH with low thromboembolic risk. These were mainly medical patients as in other studies,[15] and this mostly applies to advanced age patients without other medical conditions which justify LMWH thromboembolic prophylaxis.

In the Deheinzelin et al study,[14] overuse was 27% or 42%, according to the guideline used for measuring thromboembolic risk (Caprini store, International Union of Angiology Consensus Statement).[14]

A few cases of overdosage were detected, mainly in medical patients. One of the reasons explaining these cases is the impact of results from the MEDENOX study on medical patients, where moderate dosages did not show differences compared to the placebo, and high dosages did produce a significant reduction of VTE incidence.[24] The main clinical practice guidelines reflect these results when the practically negligible transition between moderate and high risk is considered. Specifically, in the PRETEMED guidelines,[6] dosages of moderate risk remain at a score of 4, when medical conditions are combined with other circumstances. Above this value, the high risk dosage is recommended.

A case of underdosage was also detected in general surgery. The dosage recommended for these types of patients mostly corresponded to high risk, as this mainly concerned major surgery or minor surgical procedures for those with some frequently associated risk factor. In these kinds of patients, it has been demonstrated that higher dosages of LMWH provide greater protection than lower dosages.[25]

Although LMWH thromboembolic prophylaxis was carried out correctly in ICU patients, the use of mechanical methods is recommendable for those with contraindication to drug prophylaxis. In a cross-sectional study carried out in 2003 in the ICU department of French and Canadian hospitals, very limited use of mechanical methods for patients with contraindications to drug prophylaxis was also detected. A reason may be the lack of clinical trials evaluating these methods for ICU patients or the lack of availability of these in hospitals, as stated by the authors of this study.[26]

Lastly, regarding external validity of results obtained in this study, a series of limitations should be considered.

First of all, characteristics of the hospital should be considered. This study took place in a specialty hospital, but some of the studies mentioned took place exclusively in medical hospitals or were multicentre studies, where casuistry may vary.

Likewise, to establish suitability of treatment, the reference pattern used should be available for stratification of thromboembolic risk. Even though the Consensus Conference of the ACCP is one of the most widespread, it should not be forgotten that many other guidelines are equally valid.

It is also important to know what the contraindications for LMWH prophylaxis are and what treatment to give patients with these. Unfortunately, some publications do not specify this aspect, and some studies do not even measure this variable. In our study, patients with moderate or high thromboembolic risk who had a contraindication to LMWH and were not prescribed were classified in the underuse group. This was done in this manner because in a cross-sectional study, it would be difficult to find certain

contraindications to LMWH prophylaxis (allergy to LMWH, serious thrombopenia, intense active haemorrhages) and if relative contraindications were expected (renal insufficiency, recent non-active haemorrhage, arterial hypertension); in these the risk-benefit balance of prophylaxis use would probably lean toward benefit of use.

In conclusion, thromboembolic prophylaxis works better in surgical patients than in medical patients. It would also be interesting to develop intervention strategies which optimize LMWH use. These measures should be mainly directed towards underuse detected in elevated thromboembolic risk patients admitted to medical departments.

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Appendix 1. Form for Data Collection of Medical Patients

Prophylaxis in medical patients

1. Patient information

1.1. MRN	1.4. Bed	1.7. Weight, kg
1.2. Name (initials)	1.5. Sex (F/M)	1.8. Height, cm
1.3. Department	1.6. Age (day of the cross-sectional)	1.9. Body mass index

2. Assessment of thromboembolic risk (PRETEMED guide) (assess the day of the cross-sectional)

	Adjusted weights			
	1	2	3	4
Medical conditions	Pregnancy/puerperium Significant paresis of LE as an after effect Plane flight >6 h	Neoplasia CCI CRF-nephrotic syndrome Serious acute infection Thrombophilia*	Decompensated COPD ACVA with LE paralysis	Admitted AMI
Drugs	Tamoxifen Raloxifene Hormonal replacement therapy Oral contraceptives	Chemotherapy		
Conditions or local manipulations	Central venous catheter	Previous DVT-VTE Splint/bandage on LE due to trauma		
Others	Age >60 Obesity (BMI >28) Smoking (>30 cigarettes/day) Institutionalization	Bedridden >4 days		

ACVA indicates acute cerebrovascular accident; AMI, acute myocardial infarction; CCI, congestive cardiac insufficiency; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure (serum creatinine >2 mg/dL); DVT-VTE, deep vein thrombosis or venous thromboembolism; LE, lower extremities.
*Individually considered.

Others (specify. Do not reach score):

Calculation of adjusted risk (AR)

	Value	**AR value (sum of values)**
Medical conditions (grey): minimum 1		
Other risk circumstances (the rest)		

Recommendation

AR	**Recommendation**
1-3	Consider the use of physical measures
4	Moderate LMWH prophylactic dosage (if the scoring is reached by combining medical conditions with other circumstances) High LMWH prophylactic dosage (if the scoring is reached only by considering medical conditions)
>4	High LMWH Prophylactic dosage

LMWH indicates low-molecular-weight heparin.

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Appendix 1. Form for Data Collection of Medical Patients *(Continuation)*

3. Other thromboembolic prophylaxis methods (assess during admission and on the discharge report)
- 3.1. Physical (intermittent pneumatic compression, bandage, gradual compression stockings, Tredelemburg position)
- 3.2. Platelet antiaggregants (ASA, clopidogrel, ticlopidine, triflusal, dipiridamole, others)

4. Possible contraindications to heparin use (assess the cross-sectional day with equal measure whether the patient receives LMWH or not)
- 4.1. Allergy to heparin
- 4.2. Thrombopenia (value)
- 4.3. Recent haemorrhage (specify type)
- 4.4. Active gastroduodenal ulcer
- 4.5. Coagulation disorder (specify type)
- 4.5.1. INR (value)
- 4.5.2. aPTT (value)
- 4.5.3. Prothrombin ratio (value)
- 4.6. Acute bacterial endocarditis
- 4.7. Trauma or recent surgery of the eye or the central nervous system
- 4.8. Uncontrolled arterial hypertension ≥3 days (SAP >20, DAP >12)
- 4.9. Renal function (baseline creatinine value)
- 4.10. Others (specify)

LMWH treatment guideline (if applicable)

5. Guideline used
- 5.1. Type of dosage
  - 5.1.1. Moderate risk dosage
  - 5.1.2. High risk dosage
  - 5.1.3. Very high risk dosage
- 5.2. The same guideline is maintained for the whole period.
  - 5.2.1. Yes
  - 5.2.2. No
- 5.3. Dosage coincides with what is recommended according to risk
  - 5.3.1. Yes
  - 5.3.2. No

6. Duration of treatment
- 6.1. Beginning date
- 6.2. Ending date
- 6.3. Date of hospital discharge
- 6.4. Reason for ending

End of prophylaxis

Others (change to treatment dosage, change to another prophylactic treatment, adverse reaction, death, others)

7. Safety (assess during the whole treatment period)
- 7.1. Haemorrhage: specify (retroperitoneal, intracranial, intraocular, digestive, haematemesis, rectal bleeding, epistaxis, haematuria, gingival haemorrhage…)
  - 7.1.1. Requires transfusion
  - 7.1.2. Causes a serious or potentially mortal clinical event, or requires medical or surgical intervention to control it
  - 7.1.3. Causes a haemoglobin decrease ≥2g/dL
  - 7.1.4. Causes LMWH treatment suspension
- 7.2. Thrombocytopenia (value/s)
- 7.3. Others

Appendix 2. Stratification of Thromboembolic Risk in Patients From General Surgery, Traumatology, and in Medical Patients

Major surgery:
- With additional risk factors: high LMWH prophylactic dosage
- Without additional risk factors:
  - >40 years: high LMWH prophylactic dosage
  - <40 years: moderate LMWH prophylactic dosage

Minor surgery:
- With additional risk factors:
  - >40 years: high LMWH prophylactic dosage
  - <40 years: moderate LMWH prophylactic dosage
- Without additional risk factors:
  - >60 years: high LMWH prophylactic dosage
  - 40-60 years: moderate LMWH prophylactic dosage
  - <40 years: does not need prophylaxis with LMWH

Multiple trauma: high LMWH prophylactic dosage
Elective surgery of the hip and knee: high LMWH prophylactic dosage
Traumatic surgery of the pelvis, hip, and LE: high LMWH prophylactic dosage
Conservative treatment of LE fractures:
- >40 years:
  - With risk factors: high LMWH prophylactic dosage
  - Without risk factors: moderate LMWH prophylactic dosage
- <40 years without other risk factors: does not need LMWH prophylaxis

Arthroscopic surgery of the knee:
- >40 years:
  - With 3 or more risk factors or with previous VTE antecedents: high LMWH prophylactic dosage
  - Without risk factors: moderate LMWH prophylactic dosage
- <40 years without other risk factors: does not need LMWH prophylaxis

LE trauma with lesions to ligaments and soft parts:
- >40 years:
  - With 3 or more risk factors or with previous DVT-VTE antecedents: moderate LMWH prophylactic dosage
- <40 years without other risk factors: does not need LMWH prophylaxis

	Adjusted weights			
	1	2	3	4
Medical conditions	Pregnancy/puerperium Significant paresis of LE as an after-effect Plane flight >6 h	Neoplasia CCI CRF-nephrotic syndrome Serious acute infection Thrombophilia*	Decompensated COPD ACVA with LE paralysis	Admitted AMI
Drugs	Tamoxifen Raloxifene Hormonal replacement therapy Oral contraceptives	Chemotherapy		
Conditions or local manipulations	Central venous catheter	Previous DVT-VTE Splint/bandage on LE due to trauma		
Others	Age >60 Obesity (BMI >28) Smoking (>30 cigarettes/day) Institutionalization	Bedridden >4 days		

ACVA indicates acute cerebrovascular accident; AMI, acute myocardial infarction; BMI, body mass index; CCI, congestive cardiac insufficiency; COPD, chronic obstructive pulmonary disease; CRF, chronic renal insufficiency (serum creatinine >2 mg/dL); DVT-VTE, deep vein thrombosis or venous thromboembolism; LMWH, low-molecular-weight heparins; LE, lower extremities.
*Individually considered.

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Appendix 2. Stratification of Thromboembolic Risk in Patients From General Surgery, Traumatology, and in Medical Patients *(Continuation)*

Combinations of risk factors and recommendations

Calculation of adjusted risk (AR)

AR = sum of weights of different medical conditions (dark grey) + sum of weights of other risk circumstances (light grey)

This formula cannot apply if your patient does not present with at least one medical condition

Recommendations of VTE prophylaxis

Adjusted risk	Recommendation	
1-3	Consider the use of physical measures	
4	Physical measures or LMWH (standard dosage)	If the scoring is reached by combining medical conditions with other circumstances
	LMWH (high dosage)	If the scoring is reached only by considering medical conditions
>4	LMWH prophylaxis (high dosage)	