Prospective Registry of Diagnostic Strategies Applied on Venous Thromboembolism in Intensive Care Units of Santa Fe

CARLOS A. BECKER[1, 2], RICARDO A. FERNÁNDEZ[1, 2], JORGE PAOLANTONIO[2], MARIO LERMAN[3], ENRIQUE G. UCEDO[4], RAFAEL ÁVILA[1], FERNANDO F. FACCIO[2], CRISTIAN E. BOTTA[5], NÉSTOR CARRIZO[5], CARLA I. OBAID[6], on behalf of the investigators of the Registry of Venous Thromboembolism in Intensive Care Units in Santa Fe

ABSTRACT

Background
Venous thromboembolism is a common disease with high morbidity and mortality which can be reduced drastically with early diagnosis and treatment. The diagnosis of venous thromboembolism faces two difficulties: the low clinical suspicion and the complexity of the technical resources required which are not always available, making it difficult to apply the algorithms recommended by the guidelines.

Objectives
To evaluate the diagnostic strategies used by the intensive care units in the city of Santa Fe when venous thromboembolism is suspected, to identify if any diagnostic algorithm is applied and the final degree of diagnostic uncertainty.

Methods
A prospective multicenter and observational registry of patients hospitalized with suspicion for venous thromboembolism [(deep vein thrombosis (DVT) and/or pulmonary embolism (PE)] was elaborated by all the adult intensive care units of the city of Santa Fe.

Results
Over a 3 and a half-month period, 3042 patients were hospitalized in the 19 intensive care units of the city. Venous thromboembolism was suspected in 83 patients (50 PE, 10 DVT and 23 PE + DVT). The diagnosis was confirmed in 25 (30.1%), was ruled out in 33 (39.8%) and remained uncertain in 25 (30.1%). The final diagnostic uncertainty was 25.7% in private centers and 66.6% in public hospitals. The index of suspicion was 2.7% (range 0.9% to 8.8%). Clinical guidelines or consensuses were not systematically used.

Conclusions
This registry showed a low global index of suspicion for venous thromboembolism, the algorithms recommended by guidelines were not used and the final diagnostic uncertainty was 30.1%.

REV ARGENT CARDIOL 2014;82:203-209. http://dx.doi.org/10.7775/rac.v82.i3.1692

Abbreviations   >

PI	Principal Investigator		**VTE**	Venous thromboembolism
ICA	Intensive care area		**DVT**	Deep vein thrombosis
SI	Subinvestigator		**CCU**	Coronary Care Unit
PE	Pulmonary embolism		**ICU**	Intensive Care Unit

[1] Hospital José María Cullen, Santa Fe
[2] Sanatorio San Jerónimo, Santa Fe
[3] Instituto del Diagnóstico, Santa Fe
[4] Sagrada Familia, Santa Fe
[5] Coronary Care Unit, Clínica de Nefrología y Enfermedades Cardiovasculares, Santa Fe
[6] Sanatorio Garay, Santa Fe

INTRODUCTION

Venous thromboembolism (VTE) is a common condition with high morbidity and mortality when pulmonary embolism (PE) develops. Pulmonary embolism accounts for 10% of hospital deaths and 5% of adult deaths. (1-6) Early diagnosis and anticoagulation treatment produce a drastic reduction in mortality. (7, 8)

The diagnosis of VTE faces two difficulties: (9) firstly, the frequency with which this diagnosis is not clinically suspected, even in severe cases. There are frequent necropsy studies of hospitalized patients who died of PE without premortem suspicion of the condition. (1-3, 10, 11) Secondly, the difficulties in dealing with a positive or negative diagnosis with an adequate level of certainty, due to the fact that the diagnostic methods are costly. Lack of availability of these resources is the reason why the algorithms proposed by the guidelines (12-16) are usually inaccessible, reducing the possibility of achieving a precise diagnosis.

The aim of the present study was to evaluate the diagnostic strategies applied when VTE is suspected in public and private intensive care areas (ICA) of the city of Santa Fe. Also, the different algorithms used in different units were determined, as well as the level of diagnostic certainty reached and the time required for the diagnosis. All ICA were asked to participate in a city with more than 400 000 inhabitants.

METHODS

A prospective, multicenter and observational registry was designed, recruiting all the patients hospitalized in the adult ICA of the city of Santa Fe in whom VTE [deep vein thrombosis (DVT) and/or PE] was suspected. All the coronary care units (CCU) and intensive care units (ICU) of the city were asked to participate in the registry, in order to include all the patients hospitalized in ICA with suspected VTE or those in whom VTE was suspected during hospitalization. This registry was planned for a 3-month period, which could be extended if more patients were needed and there were no logistic issues.

Registry objectives
Primary
1. To estimate the number of cases with suspected VTE (DVT and/or PE) and the index of suspicion (percentage of suspected cases divided by all hospitalized patients) in each ICA and in all the city of Santa Fe.
2. To estimate the level of certainty achieved in the diagnosis of VTE (confirmed, ruled out and uncertain) according to the criterion of the principal investigator in each unit.
3. To estimate the percentage of cases with suspected PE in whom the algorithms recommended by the guidelines were used.

Secondary
1. To identify the causes associated with uncertain diagnoses.
2. To estimate the time taken between the diagnostic suspicion and the final diagnostic certainty (confirmed or ruled out).
3. To identify if any unit used its own diagnostic algorithm (defined as a routine diagnostic sequence used in a unit).
4. To estimate the spontaneous use of the Wells score and the Geneva score in the different units.
5. To compare the index of suspicion between public and private units, the diagnostic methods used and the level of certainty reached.
6. To assess the infrastructure available for the diagnosis of VTE in the city and in each public and private institution.

Patients admitted to ICA with a confirmed diagnosis of VTE were not recruited so as not to distort the aim of evaluating the diagnostic process. When PE was suspected at the emergency department of these institutions, the patient was always transferred to a CCU or an ICU, and the diagnosis was made in these units, recruiting the patient for the present registry.

At the same time, data from all the patients hospitalized in these units during the study period were recorded, including age, sex and diagnosis at admission. Patients were identified only by the initials of their surname and name, unit and date of admission, all under strict confidentiality.

Each ICA assigned a principal investigator (PI) and a subinvestigator (SI) in charge of the logistics and local coordination of the study. An ad hoc form was developed for each patient and, at the same time, all the patients admitted in each unit were recorded on a worksheet. The PI and the SI from each unit met every fifteen days and all the investigators met once a month to analyze the partial results up to that moment.

The diagnostic studies were performed in each institution in a decentralized fashion.

The investigators were encouraged to adopt the scheme presented in Table 10 of the European Society of Cardiology guidelines about the validated diagnostic criteria to assess PE in hemodynamically stable patients according to their clinical probability. (12)

The use of known diagnostic algorithms was explored by analyzing the diagnostic sequence used in each patient´s form and by asking the PI from each center.

Proportions and risks were calculated with their corresponding 95% confidence intervals. Continuous variables with non-normal distribution were expressed as median and interquartile range. The variables with normal distribution were expressed as mean and standard deviation and were compared using the t test. Categorical variables were expressed as percentages and compared using the chi-square test or Fisher's exact test, as applicable. In all cases, a significance α level equal to 0.05 was considered. All calculations were performed using PASW Statistics 18.0 software package.

RESULTS

The registry started on September 15, 2010 and ended on December 31, 2010 of the same year (3 months and a half). Initially, 17 of the 19 ICA of the city of Santa Fe participated, and the remaining 2 were incorporated 30 days later.

Table 1 A and B show ICA, discriminated in public or private CCU and ICU, number of beds and level of complexity available in each institution.

Two 64-row multislice computed tomography scanners were available in our city during the study period at other institutions which do not have hospitalization units. Quantitative ELISA for D-dimer de-

Table 1.

A. Intensive care areas for adults in the city of Santa Fe (type of unit with its corresponding number of beds)

Type of service	Type of institution (number of beds)		Total
	Public (Hospital)	Private	
CCU	1 (11)	7 (57)	8 (68)
ICU	2 (24)	9 (62)	11 (86)
Total	3 (35)	16 (119)	19 (154)

B. Complexity available in the 19 Intensive care areas in the 12 institutions with hospitalization units.

Type of institution (*)	CCU	ICU	HS DD.	Venous Doppler ultrasound	Ventilation / perfusion scintigraphy	CCL	TEE	MSCT	DHCT	SSCT	Doppler echocardiography
Public 1 and 2	Yes	Yes	No	Yes	No	Yes	No	No	No	Yes	Yes
Private 3 and 4	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Private 5 and 6	Yes	Yes	No	Yes	No	Yes	No	No	Yes	No	Yes
Private 7 and 8	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No	Yes
Private 9 and 10	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	No	Yes
Private 11 and 12	Yes	Yes	No	Yes	Yes	Yes	No	No	No	Yes	Yes
Private 13 and 14	Yes	Yes	No	Yes	No	Yes	Yes	No	No	Yes	Yes
Private 15	Yes	No	No	Yes	No	Yes	No	No	No	No	Yes
Public 16	No	Yes	No	Yes	No	No	No	No	No	No	Yes
Private 17	No	Yes	No	Yes	No	No	No	No	No	No	Yes
Private 18	No	Yes	No	No	No	No	No	No	No	No	No
Private 19	No	Yes	No	Yes	No	No	No	No	No	No	Yes

CCU: Coronary care unit. ICU: Intensive Care Unit. HSDD: Quantitative D-dimer by ELISA. CCL: Cardiac catheterization laboratory. TEE: Transesophageal echocardiography. MSCT: Multislice computed tomography scanner. DHCT: Double-helical computed tomography scanner. SSCT: Single-slice helical computed tomography scanner.
(*) The number in the type of institution corresponds to the identification of each of the 19 participating centers.

termination is available in only one Hematology unit outside these institutions, which provides hematology care to 4 private hospitals (with 8 ICA).

During the recruitment period, 3042 patients were admitted to intensive care and VTE was suspected in 83. Overall index of suspicion was 2.7% (0.9% - 8.8%) (Table 2). The 3 centers with the highest index of suspicion belonged to private hospitals, 2 ICU and 1 CCU. The center with the lowest index of suspicion was a private ICU. There were no significant differences in the index of suspicion between CCU and ICU (p = 0.577).

Mean age of the 83 patients was 64.3 years with a median age of 68 years (range 14-91). Seventy-four percent of suspected cases were women (in 13 units). Of the 83 suspected cases, 50 corresponded to PE, 10 to DVT and 23 to DVT + PE.

A score was used to estimate the pretest probability for PE in 16 of the 73 cases with this suspicion (21.9%); the Wells score was the most commonly used

(12 patients).

According to each PI, the diagnosis of VTE was confirmed in 25 patients (30.1%), was ruled out in 33 (39.8%) and remained uncertain in 25 (30.1%) (Table 3). Diagnostic uncertainty (25/83) was due to death before performing the diagnostic tests in 5 cases, in one patient with cancer, the relatives refused to authorize the tests and in 3 cases the patients could not undergo the tests due to their particular conditions (patients with morbid obesity in mechanical ventilation). Other causes included decision of the attending physician in one case, lack of infrastructure in 3 and unknown reasons in 12. In the 5 patients who died before undergoing the diagnostic tests, the procedures were not performed in 4 cases as cardiopulmonary arrest developed very soon and the fifth case was a patient treated as PE since admission due to difficulties in performing the angiography.

The final diagnostic uncertainty (Table 4) was greater in public [66% (6/9)] compared with private

ICA	N° of beds	Month 1 (*)	Month 2 (*)	Month 3 (*)	Last fortnight (*)	Total (*)	Suspicion (%)
1	16	79 (2)	75 (1)	78 (0)	47 (0)	279 (3)	1.1
2	11	57 (1)	41 (2)	45 (1)	21 (1)	164 (5)	3.0
3	7	38 (3)	47 (3)	18 (3)	19 (0)	122 (9)	7.4
4	9	69 (4)	65 (8)	48 (3)	40 (1)	222 (16)	7.2
5	9	68 (2)	58 (0)	47 (0)	19 (0)	192 (2)	1.0
6	7	57 (0)	46 (3)	46 (1)	35 (1)	184 (5)	2.7
7	9	30 (0)	34 (0)	31 (1)	11 (0)	106 (1)	0.9
8	9	68 (1)	66 (1)	78 (0)	33 (1)	245 (3)	1.2
9	8	13 (5)	33 (2)	29 (1)	16 (0)	91 (8)	8.8
10	8	43 (1)	42 (2)	39 (2)	21 (0)	145 (5)	3.4
11	7	23 (0)	20 (0)	26 (0)	12 (2)	81 (2)	2.4
12	10	91 (4)	102 (1)	56 (0)	33 (1)	282 (6)	2.1
13	6	42 (1)	51 (0)	49 (0)	20 (0)	162 (2)	1.2
14	6	67 (1)	42 (1)	50 (0)	17 (0)	176 (2)	1.1
15	8	82 (5)	71 (0)	50 (1)	28 (0)	231 (6)	2.6
16	8	23 (1)	26 (0)	24 (0)	10 (0)	83 (1)	1.2
17	8	47 (0)	40 (2)	45 (0)	22 (0)	154 (2)	1.3
18	4	0 (0)	23 (1)	22 (1)	14 (0)	59 (2)	3.4
19	4	0 (0)	25 (1)	27 (2)	12 (0)	64 (3)	4.7
Total	154	897 (31)	907 (28)	808 (16)	430 (8)	3042 (83)	2.7

Table 2. Hospitalizations in intensive care areas, by month and overall, with identification of suspicion for venous thromboembolism. Estimation of suspicion index for each unit and global

(*): n of hospitalizations (n of suspected cases).

Center	Total	Suspected	Confirmed	Ruled out	Uncertain	Uncertain %
ICU	1393	35	11	12	12	34.3
CCU	1649	48	14	21	13	27.1
Total	3042	83	25	33	25	30.1

Table 3. Distribution of patients per ICU and CCU, according to total and suspected cases, discriminated in confirmed, ruled out and uncertain diagnoses

CCU: Coronary care unit. ICU: Intensive Care Unit.

ICA [25.7% (19/74)] [(p = 0.023) OR 5.79 (95% CI 1.12-33.03)].

The time taken to define a precise diagnosis since VTE was suspected was 1.5 days (range: 1 to 6 days) in the patients in whom this diagnosis was confirmed or ruled out.

The diagnostic test most commonly indicated in patients with suspected VTE (DVT and/or PE) was venous Doppler ultrasound in 50 patients (58.8%), followed by transthoracic Doppler echocardiography in 31 patients (37.3%). The third place corresponded to ventilation-perfusion scintigraphy in 21 cases (25.3%), followed by pulmonary angiography in 12 (14.4%). Double-helical computed tomography scan was performed in 8 patients (9.6%) and D-dimer in another 8. D-dimer was indicated in only 2 units either using the latex test in one or ELISA in the other (Table 5).

Diagnostic algorithms recommended by the guidelines were not used and neither was a self-developed algorithm followed.

Table 4. Diagnostic uncertainty according to public and private intensive care areas

	Public	Private	Total
Uncertain	6	6	6
W/diagnostic accuracy	3	3	3
Total	9	9	9

DISCUSSION

The present registry has two distinctive features: firstly, it incorporated patients with suspected DVT or PE with the aim of evaluating the diagnostic process, as opposed to traditional registries, as the ICOPER and the RIETE registries, which included only patients with a confirmed diagnosis. (17, 18) Secondly, the index of suspicion for VTE in all the patients hospitalized in ICU and CCU in the city could be estimated, as the registry included all the ICA in a city with more than 400,000 inhabitants.

However, some limitations should be mentioned:

Table 4. Diagnostic tests ordered in case of suspicion for venous thromboembolism

	VDU	DEcho	V/Q S	P Ang	D-dimer (*)	DHCT
ICU (35)	22	15	7	8	0	1
CCU (48)	28	16	14	4	8	7
Total (83)	50 (58.8%)	31 (37.3%)	21 (25,3%)	12 (14.4%)	8 (9.6%)	8 (9.6%)

(*) D-dimer: 4 quantitative D-dimer by ELISA and 4 by latex test. CCU: Coronary care unit. ICU: Intensive Care Unit. VDU: Venous Doppler ultrasound. DEcho: Doppler echocardiography. V/Q S: Ventilation/perfusion scintigraphy. P Ang: Pulmonary angiography. DHCT: Double-helical computed tomography scanner.

the study included only patients hospitalized in ICA, the period of recruitment was short (3 months and a half, 108 days) and during spring, a seasonal factor which could have conditioned a lower incidence of the disease.

Other hospitalization units besides those providing intensive care were not included due to the lack of logistics to avoid omissions in the recruitment of patients, particularly in those with final negative results. Intensive care areas provide an accessible model with the possibility of including all the suspected patients, ensuring the incorporation of all the cases.

The rate of suspicion was strikingly low (2.7/%), with important oscillations among the different units (0.9%-8.8%), and although the lowest index corresponded to an ICU from a private center, when all the private ICU were grouped and compared with the two public ICU, the latter had the lowest rate of suspicion by groups (1.0%).

Three large interventional, prospective, double blind, randomized and placebo-controlled trials, designed to demonstrate the efficacy of VTE prophylaxis in high-risk hospitalized patients, differ in the incidence of reported VTE in the placebo arm with the low incidence of suspected VTE in our registry, a difference which is higher if it is compared with the incidence of diagnosed VTE. The incidence of VTE in the placebo arm was 14.9% in the MEDENOX trial, (19), 4.96% in the PREVENT trial, (20) and 10.5% in the ARTEMIS trial. (21) When VTE prophylaxis was systematically applied in these studies, the incidence decreased to 5.3%, 2.8% and 5.6%, respectively. Our incidence of VTE was 0.8% (25 patients of 3042 hospitalized patients).

The low incidence of VTE in our registry, compared to that reported in these 3 prospective trials, might be due to the strategies used to identify the condition: VTE tests were systematically used in the three prospective studies, with a high proportion of asymptomatic cases of DVT and PE. In our registry, only patients with clinical suspicion were evaluated. The distribution of the diseases that caused hospitalization may be another possible explanation.

The inadequately low clinical suspicion has also been documented in the necropsy series mentioned in the introduction, where most of the fatal cases had not been suspected by the attending physician during hospitalization. (1-3, 10, 11)

In our study, there was a trend towards higher suspicion of VTE in women, in agreement with the study of Beam et al. (22) who ordered PE tests more frequently in women without finding a hypothesis for this gender difference. As in that study, this phenomenon was observed in most of the units participating in our registry.

The algorithms recommended by the guidelines were not used and none of the units followed their own algorithm.

The investigators of this registry (also coordinators in their respective ICA) were aware of the algorithms proposed for the diagnosis of PE, so this was not the reason why the guideline recommendations were not applied.

Venous Doppler ultrasound was indicated in 50 patients (58.8%), followed by transthoracic Doppler echocardiography in 28 patients (32.9%). Only a few units used transthoracic Doppler echocardiography as part of the diagnostic sequence.

Several reasons can explain the lack of use of multislice or helical computed tomography scans in this registry: 1) none of the multislice scanners available in our city belonged to the institutions with hospitalization units, and the patients had to be transported outside the ICA to undergo the study; 2) lack of medical coverage for patients in the public health care system and for those under some social security coverages; 3) suspicion of DVT without PE in some patients; and, 4) the low probability in other patients in whom the diagnosis could be ruled out by quantitative ELISA for D-dimer determination or ventilation/perfusion scintigraphy. A significant group of patients who were candidates for computed tomography scans should have been studied using this method.

The diagnosis of VTE was confirmed in 25 of the 83 patients (30.1%), a percentage similar to that published by other authors who confirmed the diagnosis of PE in 24% to 35% of suspected patients. (23-28) The diagnosis was uncertain in 30.1% (25 patients) of the suspected cases and in 13 of them the causes that interfered with the final diagnosis were identified.

CONCLUSIONS

The present registry exposes an alarming reality by showing a strikingly low index of suspicion and inadequate diagnostic strategies, with disparity of resources between the public and the private health care system and arbitrary and irregular use of these resources. This situation motivated the participants

of this registry to correct the low index of suspicion, to apply the algorithms proposed by the guidelines and to optimize the available resources.

RESUMEN

Registro prospectivo de estrategias diagnósticas implementadas para tromboembolia venosa en servicios de medicina intensiva

Introducción

La tromboembolia venosa es una enfermedad frecuente con una morbimortalidad elevada, que puede reducirse en forma drástica cuando la condición se reconoce y trata precozmente. Su diagnóstico tropieza con dos dificultades: la baja sospecha clínica y la complejidad de los recursos técnicos requeridos no siempre disponibles, lo que dificulta la aplicación de los algoritmos propuestos en las guías.

Objetivos

Evaluar las estrategias diagnósticas en los servicios de cuidados intensivos de la ciudad de Santa Fe ante la sospecha de tromboembolia venosa, identificar si se utiliza algún algoritmo diagnóstico y el grado de incertidumbre diagnóstica final.

Material y métodos

Se convocó a todos los servicios de cuidados intensivos para adultos de la ciudad de Santa Fe para la elaboración de un registro prospectivo, multicéntrico y observacional con el reclutamiento de los pacientes internados con sospecha de tromboembolia venosa [(trombosis venosa profunda (TVP) y/o tromboembolia pulmonar (TEP)].

Resultados

En un período de 3 meses y medio se internaron 3.042 pacientes en los 19 servicios de cuidados intensivos de la ciudad. Se sospechó tromboembolia venosa en 83 pacientes (50 TEP, 10 TVP y 23 TEP + TVP). El diagnóstico se confirmó en 25 (30,1%), se descartó en 33 (39,8%) y permaneció incierto en 25 (30,1%). La incertidumbre diagnóstica final fue del 25,7% en los servicios privados y del 66,6% en los públicos. La tasa de sospecha fue del 2,7% (rango 0,9% a 8,8%). No hubo empleo sistemático de guías clínicas ni de consensos conocidos.

Conclusiones

Este registro mostró un índice de sospecha global bajo para tromboembolia venosa, no se utilizaron los algoritmos diagnósticos propuestos en guías y consensos y el diagnóstico permaneció incierto en el 30,1%.

Palabras clave > Tromboembolismo - Diagnóstico - Epidemiología

Conflicts of interest
None declared.

REFERENCES

1. Lindblad B, Sternby NH, Bergqvist D. Incidence of venous thromboembolism verified by necropsy over 30 years. Br Med J 1991;302:709-11. http://doi.org/dtk9xm
2. Sandler DA, Martin JF. Autopsy proven embolism in hospital patients. Are we detecting enough deep vein thrombosis? J R Soc Med 1989;82:203-5.
3. Havig O. Deep vein thrombosis and pulmonary embolism. An autopsy study with multiple regression analysis of possible risk factors.
Acta Chir Scand (Suppl) 1977;478:1-120.
4. Saeger W, Genzkow M. Venous thromboses and pulmonary embolism in post-mortem series: probable causes by correlations of clinical data and basic diseases. Path Res Pract 1994;190:394-9. http://doi.org/fkz9pq
5. Karwinsky B, Svendsen E. Comparison of clinical and postmortem diagnosis of pulmonary embolism. J Clin Pathol 1989;42:135-9. http://doi.org/dmc8g4
6. Mordeglia F, Gandulla L, Bertorello M, O'Flaherty E, Gil M. Tromboembolismo pulmonar agudo: Estudio de 140 casos con comprobación necrópsica. Medicina (Bs As) 1977;32:112-26.
7. Dalen JE, Alpert JS. Natural history of pulmonary embolism. Prog Cardiovasc Dis 1975;17:259-70. http://doi.org/fwhvkc
8. Giuntini C, Di Ricco G, Marini C, Melillo E, Palla A. Epidemiology. Chest 1995;107(Suppl 1):3S-9S. http://doi.org/dvtqcf
9. Becker CA. Aspectos no resueltos en tromboembolia venosa. 6° Congreso Virtual de Cardiología por Internet 2009. Cetifac.
10. Rubinstein I, Murray D, Hoffstein V. Fatal pulmonary emboli in hospitalized patients: an autopsy study. Arch Intern Med 1988;148:1425-6. http://doi.org/fc2rkk
11. Nielsen HK, Bechgaard P, Nielsen PF, Husted SE, Geday E. 178 fatal cases of pulmonary embolism in a medical department. Acta Med Scand 1981;209:351-5. http://doi.org/dqzfps
12. The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J 2008;29:2276-315. http://doi.org/d6njpg
13. Consenso de Enfermedad Tromboembólica. Consenso Argentino SAC. Rev Argent Cardiol 2009;77:411-28.
14. Tapson VF. Acute pulmonary embolism. N Engl J Med 2008;358:1037-52. http://doi.org/bsf8vj
15. Agnelli G, Becattini C. Acute pulmonary embolism. Review. N Engl J Med 2010;363:266-74. http://doi.org/dmwj28
16. Konstantinides S. Acute pulmonary embolism. N Engl J Med 2008;359:2804-13. http://doi.org/cd93f9
17. Lobo JL, Zorrilla V, Aizpuru F, Uresandi F, García-Bragado F, Conget F, et al. Clinical syndromes and clinical outcome in patients with pulmonary embolism. Findings from the RIETE Registry. Chest 2006;130:1817-22. http://doi.org/fbnrfz
18. Goldhaber SZ, Visani L, De Rosa M for ICOPER Study Organization. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet 1999;353:1386-9. http://doi.org/cgnq4s
19. Samama MM, Cohen AT, Darmon JY, Desjardins L, Eldor A, Janbon C, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. N Engl J Med 1999;341:793-800. http://doi.org/d9hwpv
20. Leizorovicz A, Cohen AT, Turpie AG, Olsson CG, Vaitkus PT, Goldhaber SZ. Randomized, placebo-controlled trial of deltaparin for the prevention of venous thromboembolism in acutely ill medical patients. Circulation 2004;110:874-9. http://doi.org/bpsrwr
21. Cohen AT, Davidson BI, Gallus AS, Lassen MR, Prins MH, Tomkowski W, et al. Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients randomised placebo controlled clinical trial. BMJ 2006;332:325-9. http://doi.org/cwmvzf
22. Beam DM, Courtney DM, Kbarhel C, Moore CL, Richman PB, Kline JA, et al. Risk of thromboembolism varies, depending on category of immobility in outpatients. Ann Emerg Med 2009;54:147-52. http://doi.org/bh4wzz
23. Wicki J, Perneger TV, Junod AF, Bounameaux H, Perrier A. Assessing clinical probability of pulmonary embolism in the emergency ward. Arch Intern Med 2001;161:92-7. http://doi.org/fk4z7q
24. The PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED). JAMA 1990;263:2753-9. http://doi.org/frv5tx
25. The PISA-PED Investigators. Invasive and noninvasive diagnosis of pulmonary embolism. Preliminary Results of the Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISA-PED). Chest 1995;107:33s-38s. http://doi.org/b6dcx8
26. Sanson BJ, Lijmer JG, Mac Guillavry MR, Turkstra F, Prins MH, Büller HR. Comparison of a clinical probability estimate and two clinical models in patients with suspected pulmonary embolism. ANTELOPE-Study Group. Thromb Haemost 2000;83:199-203.

27. Musset D, Parent F, Meyer G, Maitre S, Girard P, Leroyer C, et al. Evaluation du Scanner Spirale dans l'Embolie Pulmonaire. Diagnostic strategy for suspected pulmonary embolism: a prospective multicenter outcome study. Lancet 2002;360:1914-20. http://doi.org/d3dt3b
28. Akram AR, Cowell GW, Logan LJA, Macdougall M, Reid JH, Murchison JT, et al. Clinicaly suspected acute pulmonary embolism: a comparison of presentation, radiological features and outcome in patients with and without PE. QJ Med 2009;102:407-14. http://doi.org/dhjrmn

APPENDIX

1. Intensive care areas for adults in the city of Santa Fe (public and private centers)*

UCO Hospital J. M. Cullen. UTI Hospital J. M. Cullen. UTI Hospital Iturraspe. UCO Instituto del Diagnóstico. UTI Instituto del Diagnóstico. UCO Sanatorio Garay. UTI Sanatorio Garay. UCO Sanatorio Mayo. UTI Sanatorio Mayo. UCO Clínica de Nefrología. UTI Clínica de Nefrología. UCO Sanatorio S. Jerónimo. UTI Sanatorio S. Jerónimo. UCO Sanatorio Santa Fe. UTI Sanatorio Santa Fe. UCO Sagrada Familia. UTI Sanatorio Americano. UTI Sanatorio Español. UTI Sanatorio Rawson.

*This order does not correspond to the number assigned to each center in the Tables or to the number of patients recruited.

2. Registry of Venous Thromboembolism in the Intensive Care Units of the City of Santa Fe

Marcelo Abud, Mario Alarcón, Marcelo Arteaga, Walter Casali, Marcelino Díaz, Atilio Giavedoni, Roberto Giménez, José Lovecchio, Fernando Marotte, Carlos Massino, María F. Otrino, Ana Pérez, Daniela Paviolo, Luis Ranieri, Martín Sánchez, Fernando Scheggia, María L. Schueri, Bruno Strada, Mariana Zavalla.