Summary

Background The wide variations in reported incidence and mortality rates reflect gaps in the epidemiology of venous thromboembolic disease (VTD), a clinical entity with two different manifestations – deep vein thrombosis and pulmonary embolism. We reviewed recent studies and data sources to find the most useful estimates of its epidemiologic indicators in France.

Methods We used international medical databases to conduct a systematic literature review. Our search focused on the incidence and mortality rates of VTD in France and examined epidemiologic studies, autopsy studies, clinical trials, and national morbidity and mortality databases.

Results The annual incidence of deep vein thrombosis is approximately 120 per 100,000 in France and 60-100 per 100,000 worldwide; the annual incidence of pulmonary embolism, the principal serious complication of deep vein thrombosis, is between 60 to 111 per 100,000 in France and between 23 and 107 per 100,000 internationally. The reported mortality rate for VTD in France is 7.2 per 100,000, but estimates from international autopsy series suggest a pulmonary embolism prevalence among hospital patients of 0.8 to 1%.

Conclusion This study demonstrates the limitations of current epidemiologic knowledge about VTD. Improved information about this disease requires better case reporting and large population-based longitudinal cohort studies.
Autopsy studies
These retrospective studies, conducted between 1960 and 1990 in patients who died in the hospital, come mainly from English-speaking and Nordic countries. Several approaches were distinguished: studies aimed only at determining the number of cases of pulmonary embolism (PE) observed during autopsy without exploring causes of death \(^{17}\)–\(^{19}\) and studies that distinguished fatal PE (direct cause of death) from those that contributed to the death \(^{20}\)–\(^{25}\). A single study \(^{26}\) separately identified incidental PE, unrelated to the death.

Treatment trials
Five large meta-analyses examined the principal clinical trials of antithrombotic prophylaxis published between 1992 and 2000. These studies assessed mortality attributable to VTD either directly, with a fatal PE rate \(^{27}\)–\(^{28}\), or indirectly, by comparing overall mortality within the patient groups \(^{27}\)–\(^{31}\).

National morbidity and mortality databases
French morbidity data for the general population come from the Credes survey \(^{32}\) (which measured household healthcare service consumption); the national medical informatics program (PMSI) compiles hospital data \(^{33}\). INSERM publishes the French cause-of-death data, based on death certificates \(^{34}\).

French epidemiologic data
Figure 1 presents the French data. Oger’s (EPI-GETBO) study \(^{4}\) was a prospective population-based study that applied exhaustive and objective criteria. It estimated the overall annual incidence of VTD at 180 per 100,000; that included an incidence of 120 per 100,000 for deep vein thrombosis (DVT) and of 60 per 100,000 for PE. The Credes survey \(^{32}\), conducted among the general population, calculated the annual incidence of DVT at 518 per 100,000; that of PE at 101 per 100,000. This estimate is very close to that from PMSI \(^{33}\) (between 96 per 100,000 and 111 per 100,000 from 1997 through 1999) for hospital populations. Dhote et al. \(^{7}\) studied patients hospitalized in internal medicine wards and calculated a DVT prevalence of 1.4% and a PE prevalence of 0.17%. In a similar setting, Bressolette et al. \(^{10}\) observed a prevalence of asymptomatic DVT at admission of 5.5%.

Other studies in France provide information about the relative frequency of DVT and of PE, as well as on risk factors for VTD. Ferrari et al. \(^{8}\) report that 52.3% of patients hospitalized for confirmed VTD had a DVT and a PE. Meignan et al. \(^{5}\) analyzed a series of lung scintigraphy studies performed systematically in patients with a phlebographic diagnosis of proximal DVT and observed that the frequency of PE without clinical events among outpatients ranged between 40 and 50%. Girard et al. \(^{3}\) observed a DVT frequency of 82% in patients for whom PE had been diagnosed; it was proximal in 60% of cases. The cause-of-death statistics from Inserm \(^{34}\) reveal that in 1999 the mortality rate attributable to PE was 7.2 per 100,000; we must add to this figure the deaths for which the recorded cause was DVT (1.9 per 1,000,000).

Principal international epidemiologic data
According to the estimates accepted by the 1997 consensus conference on the prevention of venous thromboembolic accidents \(^{35}\), the annual incidence of DVT was 160 per 100,000, that of symptomatic (but not fatal) PE 20 per 100,000, and that of fatal PE (diagnosed post-mortem) 50 per 100,000. Anderson et al. \(^{12}\) report an annual incidence of 48 per 100,000 for DVT and 23 per 100,000 for PE. Given the proportion of VTD cases that are not hospitalized, they also consider that the annual incidence of DVT in the United States general population is probably around 245 per 100,000, an estimate fairly close to that of the Canadian study \(^{11}\), but higher than that of the Swedish \(^{15,16}\) and other American \(^{13,14}\) studies. The overall rate of PE in the large autopsy series ranges from 2.5% \(^{19}\) to 31.7% \(^{21}\), and the rate of fatal PE from 2.1 \(^{20}\) to 28.9% \(^{21}\). Bergqvist et al. \(^{26}\) observed a rate of incidental (nonfatal) PE of 44.5%.

If we assume that the risk of thromboembolism for a hospitalized patient is independent of the risk of being hospitalized in case of death, we can rely on the results of autopsy studies to estimate the prevalence of PE among hospitalized patients. When we apply the global PE rate observed in the autopsy series to all of the patients hospitalized during the study period, the prevalence of PE among hospitalized patients ranges between 0.8% \(^{21}\) and 1% \(^{26}\). Figure 2 reports the mortality rate of PE observed in the principal meta-an-
lyses. Depending on the antithrombotic prophylaxis used, the overall mortality rate ranged between 0.52% and 6.5%\(^3\), and the rate of fatal PE between 0%\(^2\) and 26%\(^7\).

**Discussion**

The incidence of PE reported by the PMSI\(^3\) is quite similar to that in the Credes study\(^3\). These French estimates are fairly close to the population-based rates for other countries. On the other hand, the PE rate from the prospective population-based Epi-Getbo study\(^4\) is less than half of these. Extrapolating these figures to the French population (59,096,259 persons in 1999), with an incidence rate between 60 and 100 per 100,000 and a lethality rate of 10% indicates that PE in France accounts for 35,000 to 66,000 new cases annually and causes 3,500 to 6,600 annual deaths. The upper range of this estimate appears closer to reality. The estimates of DVT incidence are much more scattered and vary by a factor of 10; figure 1 suggests that the Credes values are strongly overestimated and that the Epi-Getbo\(^4\) study results, which are close to those of international-population-based studies, should be accepted instead.

These two manifestations of VTD – deep vein thrombosis and pulmonary embolism – are not always considered separately; depending on the study, sometimes the first event diagnosed is the one that characterizes the VTD. The variation in the methods used to detect DVT and PE often prevents comparison between studies. While prevention practices improved consistently over time, they varied from one country to another. This review summarizes available epidemiologic data about VTD, which can best be described as a patchwork quilt of varying populations, study methods and results.

**What is already known**

- Venous thromboembolic disease in its two manifestations – deep vein thrombosis (DVT) and pulmonary embolism (PE) – is recognized as a relatively frequent disease. Because of the diagnostic difficulties and morbidity and mortality associated with it, prevention is essential.
- The epidemiologic data available in France come mainly from analysis of the circumstances of onset and genetic and acquired risk factors.
- There are fewer descriptive epidemiologic studies, and it is difficult to quantify the overall population currently affected by this multifactorial condition.

**What this article adds**

- French hospital statistics provide an estimate of the incidence of pulmonary embolism similar to that of the Credes study, and these French estimates are similar to the population-based rates of other countries, all with rates nearly twice as high as those from the Epi-Getbo study.
- Pulmonary embolisms in France probably account for 35,000 to 66,000 new cases each year and cause 3,500 to 6,600 deaths annually.
- The Credes figures for the incidence of deep vein thrombosis are highly overestimated; the results of the Epi-Getbo study in western France, similar to those in other countries, should be accepted instead.

**Figure 2** Mortality rates based on the principal meta-analyses of the trials for thromboembolic risk prevention

**Conclusion**

Improvement in epidemiologic knowledge of VTD worldwide requires more uniform and exhaustive case reporting. Only large longitudinal cohort studies in the general population can supply the reference rates of incidence and mortality that are essential to any epidemiologic approach to this condition.
Epidemiology of venous thromboembolic disease

References

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