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Review Article

Thrombosis: A major contributor to global disease burden ☆

ISTH Steering Committee for World Thrombosis Day
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ABSTRACT

Thrombosis is a common pathology underlying ischemic heart disease, ischemic stroke, and venous thromboembolism (VTE). The Global Burden of Disease Study 2010 (GBD 2010) documented that ischemic heart disease and stroke collectively caused one in four deaths worldwide. GBD 2010 did not report data for VTE as a cause of death and disability. We performed a systematic review of the literature on the global disease burden due to VTE in low, middle and high income countries. Studies from Western Europe, North America, Australia, and Southern Latin America (Argentina) yielded consistent results with annual incidences ranging from 0.75 to 2.69 per 1,000 individuals in the population. The incidence increased to between 2 and 7 per 1,000 among those 70 years of age or more. Although the incidence is lower in individuals of Chinese and Korean ethnicity, their disease burden is not low because of population aging. VTE associated with hospitalization was the leading cause of disability-adjusted-life-years (DALYs) lost in low and middle income countries, and second in high income countries, responsible for more DALYs lost than nosocomial pneumonia, catheter-related blood stream infections, and adverse drug events. VTE causes a major burden of disease across low, middle, and high income countries. More detailed data on the global burden of VTE should be obtained to inform policy and resource allocation in health systems, and to evaluate if improved utilization of preventive measures will reduce the burden.

Contents

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Introduction

A doubling of life expectancy and quadrupling of the world population during the 20th century have been associated with a transition from infectious to non-communicable diseases as the major cause of death and disability worldwide [1–3]. Cardiovascular disease is a leading contributor to the burden caused by non-communicable diseases. Thrombosis is the most common underlying pathology of the three major cardiovascular disorders: ischemic heart disease (acute coronary syndrome), stroke, and venous thromboembolism (VTE).

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD Study), which was initiated by the World Health Organization and the World Bank, is a systematic scientific investigation aimed at quantifying the comparative magnitude of health loss due to diseases, injuries and risk factors by age, sex and geographic region throughout the world [3–5]. The most recent version of this effort, GBD 2010, documents the number of deaths from 235 causes from 1990 through 2010, using data from 187 countries and 21 regions; these regions are grouped further into 7 super-regions [4,5]. The study also provides estimates of the years of life lost due to premature mortality (YLL), the years lived with disability (YLD) and the disability-adjusted life years (DALYs) [4,5]. DALYs estimate how many years of healthy life are lost because of premature death or non-fatal illness or disability, and are calculated as the sum of YLL and YLD [6].

GBD 2010 documented 52.8 million deaths globally in 2010 [3]. Non-communicable disease accounted for 34.5 million deaths, or two out of every three deaths [3]. Ischemic heart disease (7.0 million deaths) and stroke (5.9 million deaths) collectively caused one in four deaths worldwide [3]. The 7.0 million deaths from ischemic heart disease represent a 35% increase since 1990. About half of all stroke deaths were from ischemic stroke, which is caused by thrombosis. The 2.8 million deaths from ischemic stroke represent a 25% increase since 1990. Although there is substantial regional variation, ischemic heart disease ranks as the number one or two causes of YLL in 13 of the 21 regions, and ranks in the top five causes of death in 17 regions [3]. Stroke ranks as the first or second cause of YLL in 8 regions, and is in the top five causes in 14 regions [3]. Ischemic heart disease was the leading cause of DALYs lost worldwide in 2010 (up from fourth rank in 1990, an increase of 29%), and stroke was the third leading cause (up from fifth rank in 1990, an increase of 19%) [6]. More than 60% of new strokes, and 45% of deaths from stroke occur in individuals less than 75 years of age [7].

GBD 2010 clearly documents the major impact of arterial thrombosis on global disease burden because it is the pathological mechanism underlying most cases of ischemic heart disease and ischemic stroke. However, the study does not report data for VTE as a specific cause of death and disability. A cursory review of the literature from Western Europe and North America suggests that VTE is a major contributor to the burden from non-communicable diseases. For example, Cohen and colleagues used an incidence-based epidemiology model to estimate the number of non-fatal symptomatic VTE events, which includes both deep-vein thrombosis (DVT) and pulmonary embolism (PE), and the number of VTE - related deaths across the European Union in 2004 (population 454.4 million) [8]. The results yielded estimates of 684,019 DVT events; 434,723 PE events; and a total of 543,454 VTE - related deaths [8]. In the United States, investigators from the Centers for Disease Control and Prevention used data from the National Hospital Discharge Survey to estimate there were an average of 547,596 adult hospitalizations with a diagnosis of VTE each year during 2007 to 2009 among the population of 301 to 307 million [9]. If VTE causes a proportionate burden of disease across the other global regions, it would be highly ranked in the causes of death and DALYs worldwide. Given that much of the mortality and morbidity from VTE is potentially preventable [10–13], data on the disease burden are important for health systems and policy makers for planning resource allocation, both for health care delivery and for setting research priorities.

We therefore performed a systematic review of the literature on the global burden of disease due to VTE. The objective was to review the evidence for disease burden in each of the geographic regions specified in the GBD Study 2010, using the variables of annual incidence rate (number of new cases each year per 1,000 population at risk), prevalence (proportion of the population with the condition at a point in time), annual number of deaths, and DALYs.

Methods

Literature Search and Review

A computer search of the literature was performed using OVID Medline, OVID Medline In-Process and Other Non-Indexed Citations, and EMBASE, from inception of these databases to May 2014. We used the disease-related key words venous thromboembolism, deep-vein thrombosis, venous thrombosis, vein thrombosis, thrombophlebitis, pulmonary embolism, and lung embolism, together with the additional key words incidence, prevalence, mortality, case fatality, morbidity, surveillance and epidemiology, years lived with disability (YLD), and disability –adjusted life years (DALY), to search the titles and abstracts of articles in these databases. We also reviewed the bibliographies of published articles. We excluded non-human studies, case reports and clinical trials, as well as non-relevant publication types, including reports of clinical conferences and editorials. We also excluded articles published in languages other than English; and the current report is confined to the literature published in English. The identified citations from each database were exported to an ENDNOTE library where the citations were de-duplicated. The merged list of citations was exported to a Word document that included citation number, title, list of authors, the full abstract, and the journal citation.

The abstracts were reviewed independently by two reviewers (A.W., G.R) who categorized them according to the level of evidence as either level A, level B, or other; disagreements were resolved through discussion and consensus. Level A evidence was defined as population-based estimates of the parameters of the disease burden (incidence, prevalence, number of deaths, DALYs) in the general population (age 18 years or older) derived from either population-based cohort studies, or from analysis of national health system databases or private health insurance claims data within a defined population, or derived using a combination of the former methods with appropriate epidemiologic modeling methods. Level B evidence was defined as estimates of the burden in specific sub-populations such as the elderly, pregnancy, etc. using the same methods described for level A. The category of "Other" evidence included all other study designs without a defined population to derive the disease burden parameters, such as single hospital base cohort studies or record review, and autopsy studies. Population-based mortality studies based on hospital discharge or other databases, or