DEEP VENOUS THROMBOSIS — I

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INTRODUCTION

Deep venous thrombosis has long been a subject of paramount importance due to its relative frequency among patients in risk groups for its initial discomfort, severe incapacitation including hospitalization, unpredictable association with pulmonary emboli, the potential complication of bleeding from the prophylaxis and finally for the importance of postphlebitic incompetence.

Postoperative deep venous thrombosis is a frequently encountered complication. A significant portion of all pulmonary embolism cases are the complications of deep venous thrombosis and deaths due to pulmonary emboli occur among otherwise healthy patients who are without antecedent clinical signs of thrombosis.

It is generally considered that the earliest description of deep venous thrombosis was made by Hunter (1) in 1837 who stated that the disease was primarily an inflammation of the intimal coat. The inflammatory peripheral venous lesions were classified into two distinct disorders in 1854 by Rokitansky (1) where in one he considered that the inflammation of the vein was primary and in the other that the thrombosis was secondary. Virchow (2) in 1860 described the pathogenetic factors still considered to be sufficient and known as the classical triad. The entire subject was reviewed by Welch (1) in 1899 where he summed up the presence of various risk factors and theories on etiology. The first description of venous thrombosis as a postoperative complication was made by Strauch (1) in 1894 when 3 cases were described. Sevitt and Gallagher (3) in 1959 showed that deep venous thrombosis occurs in the veins of the lower limbs and main pelvic veins especially in the pocket of valves.

INCIDENCE

The incidence of deep venous thrombosis varies in different parts of the world for reasons that are not yet completely understood (4). It is very difficult to determine the true incidence of venous thromboembolic diseases and their sequele because according to a screening study, over 80 % of the thrombi detected are clinically insignificant and limited to the calf (3). Autopsy studies have shown that most of the pulmonary emboli are small and clinically insignificant but fatal pulmonary emboli is still a major problem (5). Complete resolution of large venous thrombi is uncommon and occurs in fewer than 20 % of cases; they usually rest in the proximal veins of the lower leg and remain as the potential focus for pulmonary emboli (3, 6).

Although it is difficult to estimate the role of an operation apart from the other risk factors such as primary disease, age and immobilization, it is doubtlessly clear that operation by itself is a significant risk factor (7). The incidence of postoperative deep venous thrombosis has been reported as 4% to 88 % (3, 8-12) in patients undergoing surgery of any kind. Indeed various risk factors or antithrombotic properties blended with different types of operations produce a wide range of incidence. Orthopedic patients are especially prone to this problem; trauma and hip surgery are the leading causative factors (8, 10, 13—17). Patients undergoing total hip replacement differ from the other surgical patients with a higher rate of isolated femoral vein thrombi and relative unresponsiveness to low dose heparin prophylaxis (18). Deep venous thrombosis was encountered in 88 % of cases after elective total knee replacement (11), the incidence was reported to be 70 % after elective hip surgery (18). Fatal pulmonary emboli has been reported in 4 % to 7 % of patients after emergency hip surgery, 0.34 % to 1.7 % of patients after elective hip replacement and 0.1 % to 0.8 % of general surgical patients (19).

Even though deep venous thrombosis incidences up to 70 % after hip surgery were reported from a study of Western origin, data with lower incidences of deep venous thrombosis after elective hip surgery from the Eastern world are available hinting a racial predilection of Caucasians to venous thromboembolic diseases for unknown reasons (9,12, 20—22). However a statistically significant difference was not encountered in a study performed on patients of different races living in the same community (23).

As it is so much of a problem with definite prophylaxis guidelines, the disorder is often understated or not taken into serious consideration (24—26).

RISK FACTORS

Recognition of the risk factors and their impact on

the postoperative course is essential in order to screen and to recommend the proper prevention. Risk factors are related to hypercoagulable states; it is appropriate to differentiate these states into primary and secondary in order to achieve a pathogenetic based concept of the disorder. Almost all primary hypercoagulable states are related to the defects in the coagulation or fibrinolytic system rather than platelet defects (27-29).

Laboratory diagnosis of these disorders do not necessarily imply a clinically overt thrombosis. The thrombotic tendency is probably compensated by a constant action of the antithrombotic mechanism until an additive risk factor emerges.

Table I. The Primary Hypercoagulable States (30)

- Antithrombin III deficiency
- Protein C and Protein S deficiency
- Disorders of the fibrinolytic system
  - Hypoplasminogemia
  - Abnormal plasminogen
  - Plasminogen activator deficiency
- Dysfibrinogemia
- Factor XII deficiency
- Lupus anticoagulant

Table II : The Secondary Hypercoagulable States (30)

- Abnormalities of coagulation and fibrinolysis
  - Malignancy
  - Pregnancy
  - Use of oral contraceptives
  - Nephrotic syndrome
- Abnormalities of platelets
  - Myeloproliferative disorders
  - PNH
  - Hyperlipidemia
  - Diabetes Mellitus
  - Heparin-induced thrombocytopenia
- Abnormalities of blood vessels and rheology
  - Conditions promoting venous statis (immobilization, obesity, advanced age, postop. state)
  - Artificial surfaces
  - Vasculitis and chronic occlusive arterial disease
  - Homocystinuria
  - Hyperviscosity (polycythemia, leukemia, sickle cell disease, increased serum viscosity)
  - Thrombotic Thrombocytopenic Purpura

Congenital deficiency of Antithrombin III (ATIII), the primary antagonist of thrombin and other activated clotting factors are inherited autosomal dominantly with an estimated incidence of 1/2000 in the general population. Acquired ATIII deficiency may follow urinary protein loss. ATIII values below 80 % of the normal value are consistently correlated with deep venous thrombosis particularly after trauma or surgery (31-32).

Protein C and Protein S deficiencies are inherited like the ATIII deficiency and these patients have an exaggerated tendency toward recurrent venous thromboembolic disorders beginning in early adulthood (33-35). Congenital or acquired disorders of the fibrinolytic system may cause impaired resolution of fibrin and tend to relate to a higher incidence of thrombotic events (30). Functional abnormalities of fibrinogen are resistant to removal by the fibrinolytic system and are associated with a tendency to bleeding as well as to thrombotic liability. Although Factor XII (Hageman factor) deficiency, does not have a bleeding tendency, it is suggested that it may cause thrombosis (30). Lupus anticoagulant, an acquired immunoglobulin caused by SLE, neoplasms or certain drugs are related with a higher risk of thrombosis (30).

The secondary hypercoagulable states are rather complex clinical conditions in which the specific pathogenesis is not known. They probably act through more than a single mechanism. Many authors have consistently expressed the high correlation between deep venous thrombosis and malignant neoplasms (24, 36—39).

How the neoplasm interferes with the well—accepted pathogenesis is not known. Older age, prolonged bed rest, major operations and heart diseases which are common in patients with neoplasms may be the causes (39,40). Although some neoplasms may present with deep venous thrombosis, it is not appropriate to search extensively for an underlying neoplasm in a patient with venous thrombosis. Results concerning sex preponderance are controversial except that venous thromboembolism occurs 10-fold more in women under age 40 most probably due to pregnancy and oral contraceptive usage (10,41—44). Deep venous thrombosis and pulmonary embolism has been reported to occur in 0.5 % of all pregnancies (43). Venous stasis and hypercoagulability causes the clot formation. Estrogenic component of the oral contraceptives is responsible for a 7-fold increase in the thromboembolic events (41). Immobilization by inducing venous statis, whether by the will of the vulnerable patients, as a form of therapy or as a sequela of a disorder is the factor commonly accepted to primarily trigger the pathogenetic mechanism (14, 12, 45-48).

Several studies some as old as 50 years, have postulated the correlation between obesity and venous thromboembolism (12, 30). The mechanism of thromboembolic events without a major risk factor almost never occurs in a child (49). Progressive increase in the incidence of thromboembolic events starts at the fourth decade when cardiovascular system disorders or cancer risks are higher (7, 8, 43). Age 60 is commonly accepted as the threshold for the increasing tendency to deep venous thrombosis (50).

Operative insult as a cause of thromboembolic events is well recognized. The risk of thrombosis depends on several factors, particularly the type and duration of operation, the underlying disease and various risk factors of the individual patient (7). Incidence of deep venous thrombosis, diagnosed by objective criteria is higher in patients with hip fractures than in general surgical or gynecological patients (3, 8, 10, 12, 15, 17,18, 41, 51, 52). It was recently shown that lumbar or epidural anaesthesia in patients undergoing total hip replacement causes hyperkinetic blood flow, lessened tendency to coagulation of blood and better preservation of fibrinolytic function to resist thrombosis (53). Prosthetic hip or knee replacements without using cement proved to be less consistent with thromboembolic events (10, 12, 15). Deep venous thrombosis risk is higher in patients in whom the limb has multiple superficial femoral veins and more than five valves between the level of the popliteal fossa and the ischial spine (54). Lateral approach to the hip was reported to cause deep venous thrombosis less frequently (8).

The high incidence of pulmonary embolism in patients with heart disease is probably secondary to decreases in the venous flow through deficient cardiac output and immobilization (43, 55). A previous episode of venous thromboembolism eventually invites a recurrent occasion in case of a subsequent insult such as an operation (7, 50). Several studies have reported a 2-fold increase in risk in all operative patients if varicose veins are present, but in some cases varicosities occur secondary to occult deep venous thrombosis (12, 50). Venous thromboembolism maybe encountered in two or more members of a family with no hemostatic abnormality and be referred to as "familial venous thromboembolism" (56). There is the consistent finding that venous thromboembolism occurs relatively less with blood group 0 (57).

Ulterative colitis, surgical infection, Cushing's syndrome, Behcet's syndrome, nutritional factors, smoking, arhtritis, chronic pulmonary disease and usage of some pharmacological agents were questioned as risk factors (30).

PATHOGENESIS

Statis, intimal injury and hypercoagulability form the classical triad that contribute to the formation of deep venous thrombosis in surgical patients (2, 58-60). Effects of general anaesthesia and supine position cause accumulation of small deposits of platelets, fibrin and red blood cells in venous valve cusp pockets or in the intramusculer sinuses of the calf (58, 59). Intimal injury is caused by vasodilatatory ef fect of vasoactive amines and general anaesthesia exposed to thrombogenic subendothelial surfaces.

In the case of a hip operation distortion of the femoral vein during intraoperative manipulation of the leg and possible damage to its endothelial lining causes high concentrations of tissue factor to circulate (18, 61). This together with postoperative statis may well explain the high incidence of femoral vein thrombosis. In spite of the general view that calf deep venous thrombosis is benign, up to 23 % may propogate into the femoral segment where risk of embolization exists (62). Impaired venous return causing decreased clearence of activated clotting factors released from the site of injury in areas of injury and low flow, decreased ATIII activity and impaired plasmin activity set up the hypercoagulable states to yield thrombus formation. These factors then tend to accumulate in slower flow areas which are dilated veins in the lower extremity (11, 60). Gradual accumulation of thrombogenetic factors eventually cause thrombus formation upon reaching a critical level. Thrombosis occurs either during or immediately after abdominal operations whereas it may take up to 9 days in the patients with hip replacements (3, 8). However the surgeon must be aware that deep venous thrombosis may have occurred up to 62 % preoperatively (63).

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