Cancer patients are characterized by an acquired thrombophilic condition predisposing to increased risk of venous thromboembolism (VTE) [1]. Former studies have probably underestimated VTE incidence, since most of them were retrospectively conducted on patients cohorts recruited before the advent of targeted therapies, or have been focusing only on objectively confirmed symptomatic VTE. Recent research, in fact, pointed out to a higher incidence of VTE in the “real-world setting” than previously reported [2]. This might be related on improvements in computed tomography scanner technology, which has increasingly led to the detection of incidental VTE on scans performed for (re)staging of disease [3] and may have been caused, as well, by the introduction of novel therapeutic approaches with detrimental effects on vascular functions [2].

In this respect, the role played by chemotherapy in cancer-related VTE is unquestionable, and both indirect and direct evidences point out to a strong association between VTE onset and timing or type of anticancer drugs used [4,5]. Indeed, the time course of VTE incidence after an initial cancer diagnosis is highest in the first 3–6 months (i.e. during possible administration of adjuvant chemotherapy), declining during remission at rates similar to those observed in the general population and increasing again at time of relapse and related treatment [6]. However, while the use of thromboprophylaxis in hospitalized patients is currently acknowledged by all major societies’ guidelines [7,8], it is still not recommended for ambulatory cancer patients receiving chemotherapy with only few exceptions, mainly represented by patients with multiple myeloma receiving thalidomide- or lenalidomide-based regimens or very selected high-risk patients with solid tumors receiving chemotherapy, in whom, according to the latest guidelines issued by the America Society for Clinical Oncology, “clinicians may consider LMWH prophylaxis on a case-by-case basis ....... Consideration of such therapy should be accompanied by a discussion with the patient about the uncertainty concerning benefits and harms as well as dose and duration of prophylaxis in this setting” [8].

This latter concept is of particular concern in those segments of the population defined as “fragile”, meaning especially the elderly in whom risk and benefit of thromboprophylaxis stands over a particularly uncertain threshold as a result of comorbidities and impaired cardiovascular function. Cancer, in fact, is becoming an increasingly common problem in elderly patients and the number of older adults seeking treatment for cancer is considerably increasing. The chemotherapy-associated prothrombotic risk associated could find a favourable ground in elderly, who due to the presence of incidental cardiovascular risk factors (hypertension, diabetes, etc.) are more likely to develop thrombotic events [9], which might ultimately impact on active treatment, quality of life and increased demand for health care-related costs.

Hence, the need for stratification techniques to identify high-risk patients who might benefit from thromboprophylaxis. Accordingly, efforts have been devoted to identify candidate biomarkers that may be used in VTE risk assessment [5,10-16]. However, no specific biomarker has been recognized, so far, as a predictor for VTE in cancer-out-patients [17]. Indeed, some of them are interesting, but poorly feasible in a general practice setting, as in the case of soluble P-selectin, thrombin generation assays, tissue factor and microparticle measurements, which can not be routinely evaluated, but require second-level test performing laboratories and/or skilled personnel [12-14,16]. Other tests might have a clinical application, such as D-dimer, which has been shown to have a predictive role in cancer-associated VTE [10,11,15], but whose value is still debated due to low accuracy and positive predictive value (PPV), which allow just a limited prediction for an individual patient [18-20]. In this respect, we must acknowledge that a large variety of D-dimer assays are commercially available and that their poor standardization makes impossible direct comparison of results obtained with different D-dimer methods [20]. Overall, the enzyme-linked immunofluorescent assays are considered the goldstandard of D-dimer testing having the highest diagnostic accuracy for
and laboratory features known to confer an increased VTE risk to cancer patients, we are witnessing a database increase in the number of variables. Accordingly, multifactorial analysis by common biostatistical techniques can be biased by low statistical power due to inadequate sample size even in the presence of large numbers. A second challenge arises from the estimation of chemotherapy effects for an extended period, as these survival outcomes may be estimated with high variability and may be difficult to interpret. This results in an urgent need for new generation of computational theories and tools to assist researchers in extracting knowledge from the growing volumes of data. Open discussion and specifically designed studies are needed to improve risk assessment models which may help identify ambulatory cancer patients who may benefit from outpatient VTE prophylaxis.

REFERENCES


