ABSTRACT

Cancer is the second leading cause of death in Spain. Collaterally, venous thromboembolism (VTE), as a complication of cancer, consumes a great part of its healthcare budget and, more importantly, it is the second cause of death in these patients. However, limited tools are available to identify high risk patients. Additionally, a simple, minimally invasive and economical diagnostic methods for bladder cancer are also lacking. For that aim, harmful techniques are used like CT scan with high radiation exposure and invasive procedures like cystoscopy. Moreover, a hypercoagulable state seems directly related to a large tumor burden and poor prognosis. The overall aim of this Doctoral Thesis is to explore the clinical utility of novel diagnostic and prognostic methods for cancer and its thrombotic complications. In the first part of this Doctoral Thesis, we focused on the role of urine miRNAs as bladder cancer biomarkers. We identified miR-29c-3p as the most stable miRNA and was therefore used as normalizer. We adjusted an ordinal logistic regression model for the diagnosis and stratification of BC using the urine miRNA expression levels of patients and controls. This model included 7 miRNAs: miR-221-3p, miR-93-5p, miR-362-3p, miR-191-5p, miR-200c-3p, miR-192-5p and miR-21-5p. In the second part of this Doctoral Thesis, we focused on the study of novel biomarkers for cancer-associated thrombosis. We analyzed the predictive potential of miRNAs and neutrophil activation markers of thrombotic events in patients with pancreatic cancer and patients with glioma and meningioma. In pancreatic cancer, we obtained a profile of 7 miRNAs (miR-486-5p, miR-106b-5p, let-7i-5p, let-7g-5p, miR-144-3p, miR-19a-3p and miR-103a-3p) able to estimate the risk of potential VTE at diagnosis with targets involved in the *pancreatic cancer* and *complement and coagulation cascades* pathways. In the study of the neutrophil activation makers, we obtained a new predictive model of VTE with calprotectin as predictor. Regarding the study of cancer-associated thrombosis in intracranial tumors, in glioma patients, we adjusted and validated a predictive model for post-surgical pulmonary embolism (PE) with 6 miRNAs: miR-363-3p, miR-93-3p, miR-22-5p, miR-451a, miR-222-3p and miR-140-3p, and another with cfDNA and myeloperoxidase as predictors. Furthermore, we combined both types of biomarkers and obtained an improved model using myeloperoxidase and miR-140-3p as predictors. In meningioma patients we fitted and validated a predictive model with 6 miRNAs: miR-29a-3p, miR-660-5p, miR-331-3p, miR-126-5p, miR-23a-3p and miR-23b-3p. In conclusion, we

propose several profiles of biomarkers for the diagnosis of bladder cancer and for the identification of oncologic patients at high risk of suffering a thrombotic event.