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Commentary

Preoperative Prediction of Node Metastases in Bladder Cancer Patients Using Genomic and Clinicopathologic Data

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Bladder cancer (BCa) is the second most common genitourinary malignancy with 81,190 estimated new diagnosis in the 2018 in the United States only (Siegel et al., 2018). Radical cystectomy (RC) with bilateral pelvic node dissection (PLND) represents the gold standard for muscle invasive BCa and for very recurrent high risk non-muscle invasive tumors (Alfred Witjes et al., n.d.). Lymph node metastases are the pathologic features with the greater impact on mortality at RC and are diagnosed in around 18.0–30.4% patients affected by localized BCa (Stein et al., 2001). However, cross-sectional imaging can only partially predict preoperatively the presence of node metastases (Moschini et al., n.d.). In this regard, after decades without improvements in the field of BCa, several progresses in the last few years are improving patients and tumor classifications, starting a new era of precision medicine in uro-oncology.

In this issue of *EBioMedicine*, Wu et al. (Wu et al., 2018) report a genomic-clinicopathologic nomogram for the preoperative identification of BCa patients affected by lymph node metastases. Authors used a model to identify mRNAs correlated with the presence of node metastases and developed a clinical nomogram integrating clinical and pathological variables. They identified five different mRNAs (ADRA1D, COL10A1, DKK2, HIST2H3D and MMP11) that were significantly correlated with the presence of lymph node metastases and they developed a classifier for the prediction of lymph node metastases with an AUC of 0.7867. This classifier was implemented with clinical pathological data such as transurethral resection T stage, radiological N status and presence of lymphovascular invasion at transurethral resection developing a final model with a C-Index of 0.9017. Both models were externally validated by the authors and a decision curve analyses was developed to assess the clinical value of the model. Authors included sub-analyses, analyzing patients with minor risk of harboring node metastases at RC: non-muscle invasive bladder cancer (AUC 0.8396) and clinical node negative (AUC: 0.8633) finding excellent AUC also in these subgroups.

A comprehensive molecular characterization of muscle invasive bladder cancer has been recently reported by The Cancer Genome Atlas (TCGA) researchers (Robertson et al., n.d.) using a multiplatform analyses to stratify muscle invasive bladder cancer patients in subgroups. These subgroups might predict survival outcomes and response to chemotherapy, immunotherapy and therefore help to individualize the best treatment for patients. These results will have a tremendous impact on diagnoses and therapies personalizing decision process in BCa patients. Considering prediction of node metastases, previous clinical models failed to predict accurately this occurrence (Kluth et al., 2015). In this setting, Seiler et colleagues (Seiler et al., 2016) presented a whole trascriptome expression profiles generated from 199 patients treated with RC and extended pelvic lymph node dissection. Authors elaborate a classifier (KNN51) for the prediction of lymph node metastases and compared it with two previously described cancer gene

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signatures (RF15 and LN20). They found an AUC of 0.82 for their model compared to and AUC of 0.62 and 0.46 of the previous models. However, authors did not include clinical or pathological features in this model.

If confirmed and validated in other series, the work of Shao-Xu Wu et colleagues (Wu et al., 2018) can consistently help physicians to individuate patients at major risk of harboring node metastases. Other potential elements that might increase the accuracy of these models and should be evaluated in future efforts in this field are the impact of histological variants (Moschini et al., 2017) and the smoking history (Crivelli et al., 2014), two elements that have been linked to the aggressiveness of the disease but were not included in this model.

Disclosure

No disclosures or conflict of interest.

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