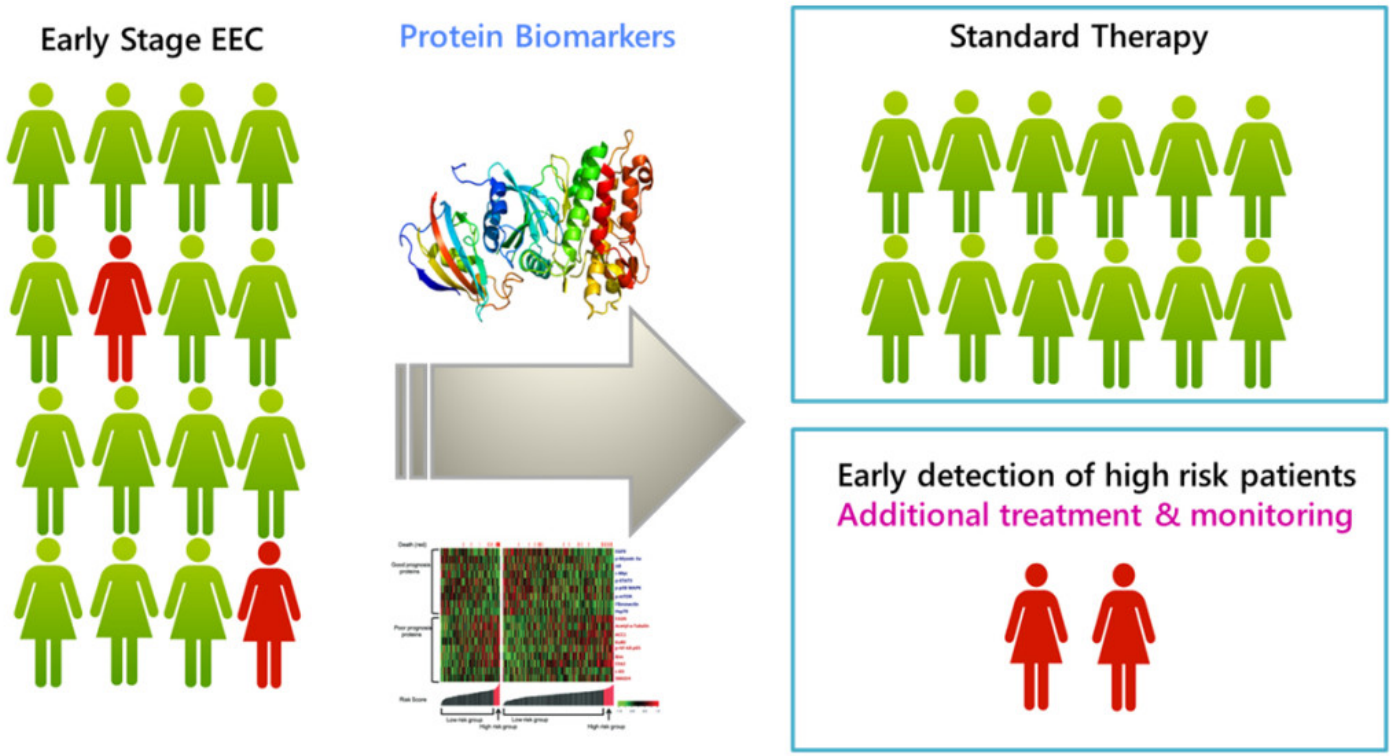
Protein expression is useful to screen high risk patients for cancer

Endometrial cancer is the most common type of uterine cancer in the United States. The American Cancer Society estimates 54,870 newly diagnosed endometrial cancer cases and 10,170 deaths caused by endometrial cancer in 2015. Most patients (~80%) have a subtype called endometrioid endometrial cancer (EEC), which is generally linked to excess estrogen, obesity and hormone-receptor positivity meaning that the growth of cancer cells are fueled by female hormones. The reported 5-year survival rate is relatively good in early-stage EEC (stage I, II, 70~90%) but it falls below 50% in late-stage EEC (40~50% for stage III, 15~20% for stage IV). Indeed, patients with late-stage EEC or recurrent disease have a poor prognosis, with a median survival rate of less than 12 months, and they are usually treated with more aggressive therapy. Fortunately, most women with EEC are diagnosed at an early stage of the disease, when the cancer can generally be cured by surgery. However, not all early-stage EEC is clinically indolent: a subset has poor prognosis due to metastasis or disease recurrence following surgery. Because of this clinical heterogeneity for early-stage EEC, it is important to identify high-quality biological indicator that can be used to stratify patients and to determine their prognoses, thereby further facilitating individualized therapeutic management of patients.



In our study, we developed a prognostic model for identifying patients with high-risk early-stage EEC, which fully utilizes clinical and proteomic features of patients. For the study, we collected 516

patient samples who were newly diagnosed with early-stage EEC from several institutions including Haukeland University Hospital (Bergen, Norway), the University of Texas MD Anderson Cancer Center (Houston, Texas, USA) and The Cancer Genome Atlas (TCGA). In order to measure relative protein expression in patients, we used proteome-based reverse-phase protein array (RPPA), which allows for a high volume of measurements in a large number of patients. Besides working as major functional units in various biological processes, many proteins are known to have the potential to reflect key processes underlying tumor development and progression that may not be captured by genes. As for the statistical method, we employed an initial filtering process and a statistical algorithm named elastic net. Our proposed model, integrating clinical information (with age and tumor grade) with proteomic profiles (with 18 proteins), showed a distinct improvement in identifying high risk patients among early-stage EEC over the models using clinical information alone. The high-risk group had a significantly shorter survival time than the low-risk group according to our model. It implies that our prognostic model is potentially of high clinical value for stratifying patients with early-stage EEC and improving their treatment strategies. Constant monitoring will be needed for high-risk EEC who is most likely to benefit from more extensive surgery and adjuvant therapy. Furthermore, this may spare patients who have low-risk EEC from potentially toxic interventions.

Publication

Integrative Protein-Based Prognostic Model for Early Stage Endometrioid Endometrial Cancer.
Yang JY, Werner HM, Li J, Westin SN, Lu Y, Halle MK, Trovik J, Salvesen HB, Mills GB, Liang H
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