REPORT
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CANCER

GENOMIC INDICATORS FOR PREDICTION OF RECURRENCE AND METASTASIS IN ENDOMETRIAL CANCER

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1. Abstract

Endometrial cancer globally is the sixth most common cancer in women and the second most common gynecological cancer. About 75-80% of cases are diagnosed at stage I with a 5-year survival rate of 95%. Unfortunately, this survival rate decreases when there is regional spread (72%) or distant metastasis (20%). Many research efforts have focused on improving early diagnosis of this disease, patient stratification, and improving treatment protocols. These protocols typically involve surgical intervention to define prognosis, and usually require the removal of the affected area and adjacent lymph nodes. This intervention (lymphadenectomy) carries risks during its execution and post-surgical complications that limit the future quality of life for patients. As a result, there is controversy regarding its anatomical extent and its diagnosis as well as therapeutic value, due to the false negatives associated with subsequent relapse. This project starts from collaborating with a team of gynecologist oncologists and biologists/bioinformaticians from the Hospital de Sant Pau in Barcelona and the IRB Barcelona. The two general objectives of the project were to develop a diagnostic and prognostic tool to determine the likelihood of recurrence in endometrial cancer patients and to evaluate the potential benefits of lymphadenectomy. To achieve this, we developed a classifier based on machine learning (ML) algorithms to predict the likelihood of recurrence based on genetic information obtained from tumor biopsies of endometrial cancer patients. This information and histopathological data have been analyzed and integrated into an ML system, enabling us to predict the most likely progression of new patients based on their genetic and histopathological information, gathered from the previous analysis of patient data for whom we have clinical outcome information. Our long-term goal is to provide a tool that assists the clinicians in designing post-surgery treatment tailored to the specific characteristics of each patient.

2. Results

Our approach combined clinical, experimental, and computational information. Samples of primary tumors from previously diagnosed patients who underwent main surgery during the past 10 years by the Hospital de Sant Pau clinical team were used. Omics Technology was performed, requiring the extraction of nucleic acids, analysis of microarray of gene expression (22,000 genes) in addition to the extraction of the

patients' clinical and histopathological information collected in the usual admission procedure. The integration of this information has allowed us to develop a software to determine the probability of relapse in these patients using mathematical algorithms of machine learning. The results of the project are twofold. First, we have obtained a classifier model that allows us to determine with 81% accuracy if a patient has a high probability of recurrence, based on information that can be easily extracted from a biopsy. Also, we have confirmed an initial hypothesis that, while lymphadenectomy, a surgical procedure with significant side effects, may have value in predicting the risk of relapse, it does not seem to have any therapeutic impact.

3. Relevance and future impact

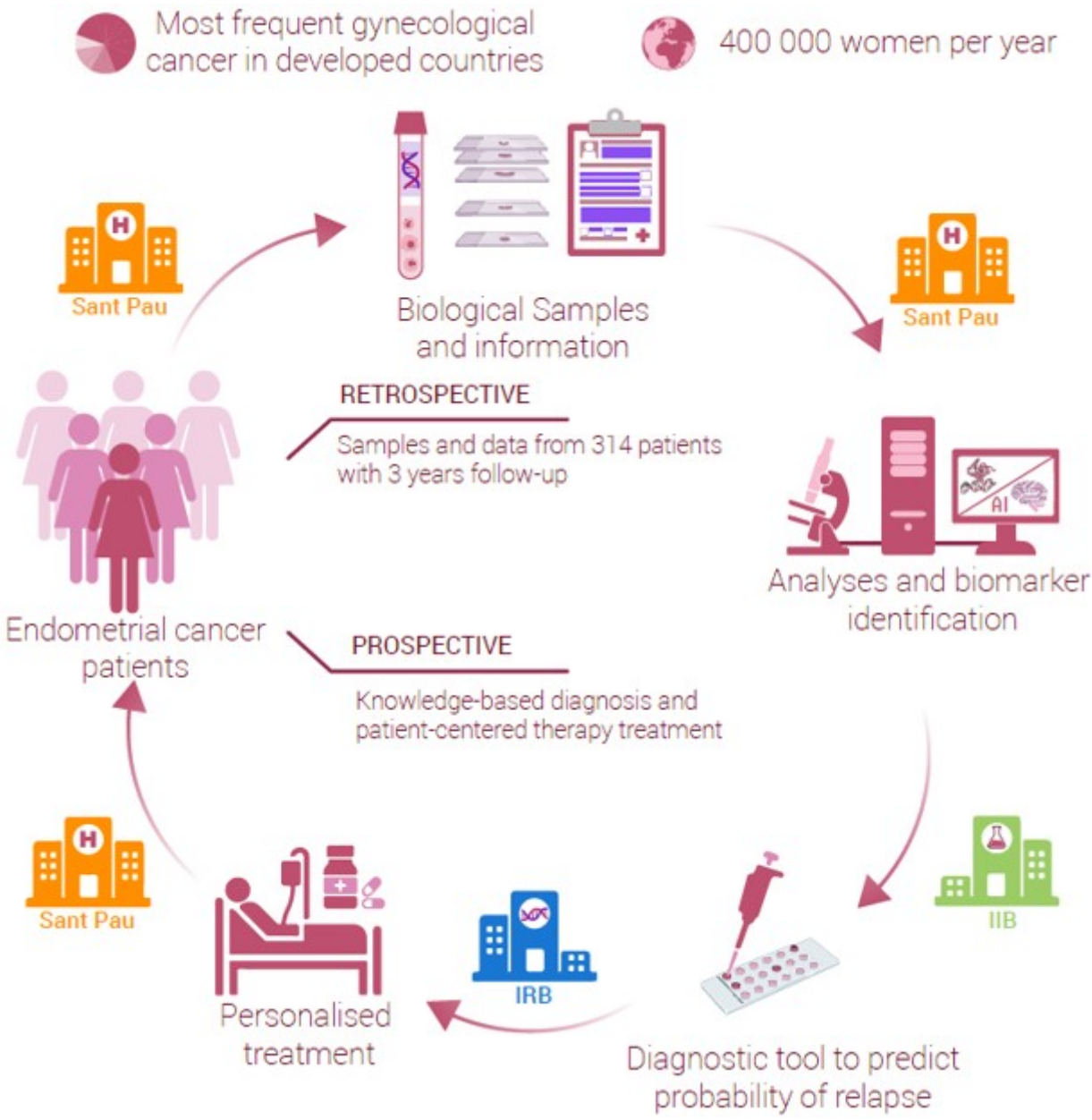
This proof of concept project focused on the group of patients from Hospital de Sant Pau, has allowed us to identify promising indicators for subsequent validation in a larger number of patients from other hospitals in our environment. In the short term, the anticipated impact of our research will be to improve the prognosis of endometrial cancer patients and their quality of life. This knowledge will be applied to each new patient before surgery, allowing us to reclassify cases considered low-risk to restrict lymphadenectomy only to beneficial cases. We aim to establish optimal and less drastic treatments for non-aggressive tumors, as well as personalized follow-ups to monitor in detail those patients with a high probability of relapse, thereby reducing the emotional cost associated with stress during follow-up, ultimately positively impacting the quality of life and patient survival. The molecular data generated through transcriptomics are, in practical terms, economically feasible for public healthcare and relatively easy to generate and analyze, representing an advantage over other approaches such as whole genomic sequencing and analysis. Anticipating possible outcomes will contribute to improving clinical medical decision-making and care, as well as resource uses. Our results will provide a complementary tool that will assist the medical team in designing treatments tailored to the specific characteristics of the patients. The identification of new molecular markers, developed software, and the annotation of patient data will also have an impact on current scientific knowledge. This knowledge can be utilized to evaluate the prognoses of other cancer patients. In the longer term, we will be able to identify molecular characteristics shared by patients with similar prognoses, which can be used as therapy targets.

4. Bibliography

We plan to validate the preliminary results in other cohorts of endometrial cancer patients to develop a final product that can be transferred to the society.
We have presented three communications at one of the most prestigious international congresses in the field of Gynecological Oncology:

the 23rd European Congress on Gynecological Oncology, 2022, in Berlin, Germany [Teixeira N et al., Factors associated with an increased risk of recurrence in endometrial cancer patients: a retrospective cohort study, and Farrés A et al., Genomic signatures for the prediction of recurrence and metastasis in Endometrial Cancer], and the 24th European Congress on Gynecological Oncology, 2024, in Barcelona, Spain [Farrés A et al., Genomic Markers For The Prediction Of Recurrence And Metastasis In Endometrial Cancers].

The project's results will lead to the development of three doctoral theses: Alba Farrés M.D, at Hospital de Sant Pau, and Rebeca A. Mees and Carles Torner at IRB Barcelona.


Most frequent gynecological cancer in developed countries
400 000 women per year
Sant Pau
Biological Samples and information
Sant Pau
RETROSPECTIVE
Samples and data from 314 patients with 3 years follow-up
AI
Analyses and biomarker identification
Endometrial cancer patients
PROSPECTIVE
Knowledge-based diagnosis and patient-centered therapy treatment
IIB
Sant Pau
Personalised treatment
IRB
Diagnostic tool to predict probability of relapse