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Original article

Cost-effectiveness of risk-reducing surgeries in preventing hereditary breast and ovarian cancer

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ABSTRACT

Objectives: Risk-reducing surgeries are a feasible option for mitigating the risk in individuals with inherited susceptibility to cancer, but are the procedures cost-effective in the current health-care system in Germany? This study compared the health-care costs for bilateral risk-reducing mastectomy (BRRM) and risk-reducing (bilateral) salpingo-oophorectomy (RRSO) with cancer treatment costs that could potentially be prevented.

Patients and methods: The analysis is based on interdisciplinary consultations with individuals with a high familial risk for breast and ovarian cancer at the University Breast Center for Franconia (Germany) between 2009 and 2013 (370 consultations; 44 patients with *BRCA1* mutations and 26 with *BRCA2* mutations). Health-care costs for risk-reducing surgeries in *BRCA* mutation carriers were calculated as reimbursements in the German diagnosis-related groups (DRG) hospital pricing system. These costs for the health-care system were compared with the potential cancer treatment costs that could possibly be prevented by risk-reducing surgeries.

Results: Long-term health-care costs can be reduced by risk-reducing surgeries after genetic testing in *BRCA* mutation carriers. The health-care system in Germany would have saved € 136,295 if BRRM had been performed and € 791,653 if RRSO had been performed before the development of cancer in only 50% of the 70 mutation carriers seen in our center. Moreover, in patients with combined RRSO and BRRM (without breast reconstruction), one further life-year for a 40-year-old *BRCA* mutation carrier would cost € 2,183.

Conclusion: Intensive care, including risk-reducing surgeries in *BRCA* mutation carriers, is cost-effective from the point of view of the health-care system in Germany.

1. Introduction

The majority of patients currently diagnosed with breast cancer (BC) or ovarian cancer (OC) have a sporadic form of the disease. Heterozygous germline mutations in either *BRCA1* or *BRCA2* are responsible for 3–8% of all cases of BC and 30–40% of familial BC cases [1–3]. In the general population the cumulative lifetime risk for BC and OC is 8–10% and 1.5–2.0%, respectively. In contrast, *BRCA1* mutation carriers have a 60–65% risk for BC up to the age of 70 and a 40–60% risk for OC. For *BRCA2* mutation carriers, the corresponding percentages are 45–55% for BC and 11–16.5% for OC [2,4]. In addition, mutation carriers have an increased risk of developing contralateral BC and relapses after initial BC treatment [5].

In our Breast and Ovarian Cancer Genetics Clinic, different medical departments (gynecology, genetics, radiology, and psycho-oncology) collaborate in an effort to optimize the evaluation and

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List of abbreviations

ASCO	American Society of Clinical Oncology
BC	Breast cancer
BRCA1	Breast cancer 1 (gene)
DRG	Diagnosis-related group(s)
GC-HBOC	German Consortium for Hereditary Breast and Ovarian Cancer
NCCN	National Comprehensive Cancer Network
NICE	National Institute for Health and Care Excellence
OC	Ovarian cancer
BRRM	Bilateral risk-reducing mastectomy
RRSO	Risk-reducing (bilateral) salpingo-oophorectomy
CRRM	Contralateral risk-reducing mastectomy
QALY	Quality-adjusted life-years

consultation for patients with hereditary BC and OC. Guidelines published by several specialist associations — including the National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology (ASCO), and the German Consortium for Hereditary Breast and Ovarian Cancer (GC-HBOC) — have defined groups of unaffected individuals in whom genetic testing is appropriate [6].

In general, risk-reducing strategies comprise intensified surveillance, lifestyle factors, chemoprevention, and risk-reducing surgeries. The risk-reducing surgical options in high-risk women include risk-reducing (bilateral) salpingo-oophorectomy (RRSO), bilateral risk-reducing mastectomy (BRRM), and contralateral risk-reducing mastectomy (CRRM) in women already diagnosed with BC. The incidence of BC in healthy *BRCA* mutation carriers can be reduced by approximately 90% through BRRM. RRSO in premenopausal women reduces not only the incidence and mortality of ovarian and fallopian tube cancer by 96%, but most studies have also shown a risk reduction for BC by approximately 50–68% [7–11].

The objectives of risk-reducing surgeries are to prevent diseases and thereby preserve health and gain life-years, but are these procedures cost-effective within the health-care system in Germany. Health-economic analyses such as cost-effectiveness analyses can help evaluate the monetary value of medical procedures and make them comparable. In cost-effectiveness analyses, life-years gained represent a possible measure for assessing the treatment benefit [12]. The life-years gained can be supplemented by costs per life-year. In general, the effectiveness of risk-reducing surgeries relative to life-years gained is strongly dependent on the age of the women at the time of surgery, suggesting that risk-reducing surgeries should preferably be carried out when the patients are younger [10].

The purpose of this study was to examine the cost-effectiveness of risk-reducing surgeries in individuals with a proven *BRCA* mutation in the context of the health-care system in Germany.

2. Methods

2.1. Study design and genetic testing

The study was conducted in the interdisciplinary Breast and Ovarian Cancer Genetics Clinic at the University Breast Center for Franconia in Erlangen, Germany. The study group (n = 370) comprised all individuals seen at our Genetics Clinic between 2009 and 2013. Data for all these individuals were collected retrospectively from their medical records. Individuals fulfilling the inclusion criteria for genetic testing were offered germline mutation testing.

2.2. Defining medical costs

Costs were calculated from the perspective of the German health care system and were presented in two ways. Firstly, all health-care costs arising for the risk-reducing surgical procedures under consideration (BRRM, CRRM, and RRSO) were calculated per person. In this process, health-care costs for risk-reducing operations in *BRCA* mutation carriers were calculated based on reimbursements in the German hospital pricing system, based on diagnosis-related groups (DRG). Secondly, all health-care costs per life-year gained for these measures were calculated.

2.3. Treatment costs for BC patients

The average total treatment costs in Germany for the initial treatment and further surveillance of patients with primary early BC, metastatic BC, and BC recurrence have previously been reported by our group [13]. These calculations considered the distribution of tumor stages and biological characteristics (e.g. grading, estrogen receptor, progesterone receptor, and Her2-status) in the German population and were used as the basis for further comparative calculations. Treatment costs of € 18,361.62 for the first year and € 20,393.74 for the first 5 years after a diagnosis of BC were taken as the basis for the calculations. In patients with recurrent BC, these treatment costs were € 15,044.01 for the first year and € 17,076.13 for the first 5 years. Overall treatment costs of € 39,028.54 for metastatic BC were assumed on the basis of previous conservative calculations by our group [13].

The average total treatment costs in Germany for the initial treatment and further surveillance of patients with primary OC, metastatic OC, and recurrent OC were calculated. These treatment costs included expenses for surgery, chemotherapy, targeted therapies, laboratory costs, diagnosis, surveillance, and palliative care. These calculations were based on the assumption that 90% of primary OC patients receive surgery first, while 10% have a tumor stage so advanced that primary cytoreductive surgery is not performed. Additional costs for potential postoperative complications were not included.

3. Results

3.1. Study group

Between 2009 and 2013, 370 individuals were seen at the interdisciplinary Breast and Ovarian Cancer Genetics Clinic at the University Breast Center for Franconia. The majority of individuals were female (n = 362, 97.8%). The average age at time of presentation was 42 years with an age range of 18–85 years.

A small proportion of individuals fulfilling diagnostic criteria opted out of genetic testing, leaving 209 individuals for genetic testing of *BRCA1* and *BRCA2* genes. Seven of the eight men who presented were tested, and 235 of the 362 women. Subsequently, 33 additional family members were also tested. Genetic testing identified 44 (19%) *BRCA1* and 26 (11%) *BRCA2* mutation carriers. Moreover, in 23 individuals (9%) variants of unknown significance were identified, seven in *BRCA1* and 16 in *BRCA2*. In total, 61% of individuals were tested completely negative for either *BRCA* gene.

At first presentation, 48 of the 70 mutation carriers already had BC and nine already had OC. Among the patients with BC, 32 (67%) had a *BRCA1* and 16 (33%) a *BRCA2* mutation. In the nine OC patients, five (56%) had a *BRCA1* and four (44%) a *BRCA2* mutation. The