How was this new, some say “radical,” concept discovered? Why are so many doctors unaware of it? And what does this new understanding of the disease mean for patients?

This discovery, first revealed in 2007, came about because of women like Hollywood actress Angelina Jolie, carriers of BRCA1 or BRCA2 mutations, who are at greatly increased risk for breast and ovarian cancers. BRCA-carriers are often treated with prophylactic bilateral salpingo-oophorectomies (surgical removal of both Fallopian tubes and ovaries) in efforts to remove the sources of cancer, which were thought to be in the ovaries. When pathologists carefully studied the tissues removed by these preventative treatments, they found precancerous conditions or early cancers in up to 17 percent of patients. But the real surprise was finding that these cancers and pre-cancers were always seen in the Fallopian tubes, and never in the ovaries.

Over the next seven years, this finding was repeatedly confirmed by medical researchers and was also extended to non-hereditary “ovarian” cancers, with critical implications for the development of new ways to screen for, prevent, and treat the disease. Gynecologists started to refer to and recommend action on this paradigm shift in 2013. In 2015, the same year that Angelina Jolie publicly disclosed that she had her ovaries removed to prevent BRCA1-related cancer, the Society of Gynecologic Oncology published new recommendations that included just removing...
the tubes alone in women who have completed childbearing in order to prevent what they were still calling ovarian cancer.

Given this new scientific understanding, it is now inaccurate and misleading to refer to the majority—and most deadly forms—of pelvic serous carcinoma (PSC) as ovarian cancer. It is also imprecise to lump all PSCs into one bucket. There is a new classification, based on characteristic features of tumor genomes, that reflects different pathways of oncogenesis, briefly:

- **Type I tumors** account for ~10-25% of PSCs and are low-grade cancers that exhibit genome stability and are usually confined to the ovary.
- **Type II tumors** account for 75% of PSCs and are high-grade cancers with unstable genomes and oncogenic, somatic TP53 mutations. These tumors develop from intraepithelial carcinoma in the finger-like projections (fimbria) of the Fallopian tubes and involve the ovary and other pelvic structures secondarily. These Type II PSCs are the ones that doctors and patients inaccurately refer to as “ovarian” cancer and typically present as advanced, metastatic disease. They account for the majority of patient deaths from PSC.
- **Hereditary** cancers account for 5-10% of PSCs and are Type II tumors caused by germline mutations in the BRCA1 and BRCA2 tumor suppressor genes.

In an age of precision medicine, we hope that doctors, administrators, insurance companies, policy makers and advocacy groups, will define and explain these conditions for the public with the appropriate accuracy and precision that women and their loved ones deserve.

Beyond semantics however, there is real harm in misleading women with an outdated terminology that impairs awareness of new possibilities for prevention and treatment while also hindering promising new avenues of research. These new approaches to a redefined disease may not only reduce the risk of pelvic serous cancers and lead to new screening methods and treatments; they may also prevent premature menopause and preserve fertility in women who now might only need to have their tubes removed, and not their ovaries, to prevent a deadly disease.

References


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