

# Synchronous Primary Endometrial and Ovarian Cancers: A Critical Update

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Synchronous primary cancers are relatively uncommon in general population [1,2]. Only 0.5-1.7% of women with gynecological malignancies, have synchronous primary cancers of the female genital tract [3-8]. In those patients, the most common combination is synchronous primary endometrial and ovarian cancers [3, 4, 6].

Patients with synchronous primary endometrial and ovarian cancers have distinct clinical characteristics including: young age, obesity, premenopausal status and nulliparity [9]. Usually, they are 10 - 20 years younger than patients with single endometrial or ovarian cancer [4,10-13]. The median age at diagnosis is 50 years [3,8,9,11-15].

The pathogenesis of synchronous primary endometrial and ovarian cancers, remains unclear[2,6,16]. The theory of the secondary Müllerian system has been proposed to explain the development of synchronous primary cancers in the female genital tract [5,6,16-18]. According to this theory, the epithelia of the upper female genital tract have common embryologic origin and respond as a morphologic unit to a carcinogenic stimulus (hormone, radiation, other) [2,5,16, 17]. Perhaps shared hormone receptors (estrogen receptors) are responsible for the development of synchronous primary cancers in the female genital tract [5,6,18].

Moreover it is possible that those patients have a more fragile genome and prior genetic damage may predispose them to the development of synchronous primary cancers [16,19-23]. Especially in patients with Lynch syndrome, there is a predisposition to multiple synchronous primary cancers (colon, endometrium, ovary, stomach, small bowel, ureter and renal pelvis) [24].

Thus embryologic, hormonal, genetic or other phenomena may be associated with the development of synchronous primary cancers of the female genital tract [5,6,16-19,21 24].

The most common presenting symptoms and signs in patients with synchronous primary endometrial and ovarian cancers, are: abnormal uterine bleeding (46%), abdominal/pelvic pain (17%) and abdominal/pelvic mass (13%) [1,2,9,11,13,15,16,25].

Synchronous primary endometrial and ovarian cancers may have similar or different histologic appearance [6,10,14]. The distinction between metastatic and synchronous primary cancers is relatively easy, when they have different histologic types [26,27]. However the distinction is relatively difficult, when they have the same histologic type [26,27]. For those patients in clinical practise we use well described empirical criteria [26,27].

The treatment of choice for most patients with synchronous primary endometrial and ovarian cancers, is systematic surgical staging [1-4 ,6,11,12,14,15,28-30]. More specifically in those patients, systematic surgical staging includes: total abdominal hysterectomy with bilateral salpingo-oophorectomy, total omentectomy, appendectomy, pelvic and para-aortic lymphadenectomy, complete resection of all disease, biopsy of any suspected lesion and pelvic washings [1,4,6,11,12,14, 28-32].

That therapeutic approach allows a more clear decision for stage related postoperative adjuvant treatment [1,2,29,30]. Moreover,

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appropriate surgical staging facilitates targeted therapy that maximize survival and minimize the morbidity of overtreatment (radiation injury, chemotherapy toxicity) and the effects of undertreatment (recurrent disease, increased mortality) [1,2,33].

Pelvic and para-aortic lymphadenectomy is essential for surgical staging in patients with synchronous primary endometrial and ovarian cancers [1,2,31,32]. It has diagnostic, therapeutic and prognostic value. It defines accurately the extent of disease and determines the prognosis of patients [1,2]. Undoubtedly, pelvic and para-aortic lymphadenectomy is the only way to identify patients with stage III disease [1,2,31,32]. However, the extension of pelvic and para-aortic lymph node dissection (more than 14 lymph nodes) is an independent risk factor for postoperative complications [1,2,29,30,34-36]. Moreover in elderly patients and in patients with relevant comorbidities (obesity, diabetes, coronary artery disease), morbidity must be carefully weighed against any survival advantage [1,2,33,37,38].

The significance of postoperative adjuvant treatment in patients with synchronous primary endometrial and ovarian cancers, remains controversial [14,15,39]. However in most cases, postoperative adjuvant treatment should be individualized according to the risk of relapse of each primary cancer [2,39,40]. Moreover, the treatment of one primary cancer does not compromise the treatment of the other primary cancer [2,41].

Especially in patients with advanced stage disease, unfavorable histologic types and high grade disease, required postoperative adjuvant treatment tailored to both tumors [1-3,6,10-12,15,25,28-30,39,41-43]. More specifically, postoperative adjuvant treatment in those patients includes: radiotherapy and/or chemotherapy [1,2,10,11 39].

Postoperative adjuvant radiotherapy includes: external pelvic radiotherapy and/or brachytherapy. It is the appropriate treatment for high risk primary endometrial cancer [1,2,29,30].

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Postoperative adjuvant chemotherapy is the appropriate treatment for advanced stage primary endometrial and ovarian cancers [1,2,40]. The most active chemotherapeutic agents for those patients, are: taxanes, anthracyclines and platinum compounds [11,15].

Prognostic factors for synchronous primary endometrial and ovarian cancers are: age, stage of ovarian cancer, grade of endometrial cancer and adjuvant treatment [43-45]. Patients with synchronous primary endometrial and ovarian cancers have 5-year overall survival 85.9% and 10 year overall survival 80.3%. 14 Patients with synchronous primary endometrial and ovarian cancers have better overall survival than patients with single primary ovarian or endometrial cancer [1,2,9,39,41,43,46]. Moreover, patients with synchronous primary endometrial and ovarian cancers endometrioid type have better overall survival than patients with non-endometrioid or mixed histologic types [1,2,9,39,43].

The reason for the better overall survival of those patients, is not intuitively obvious [1,2,14]. Perhaps favorable prognosis related with the detection of patients at early stage and low grade disease [1-3,6,20-22,25,28,46,47]. Moreover, the influence of the postoperative adjuvant treatment needs to be further investigated [39].

## Competing Interests

The authors declare that they have no competing interests.

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