Response

In their correspondence, the Mayo Clinic group expressed concern that our randomized study could be misinterpreted and commented on three study limitations that we addressed in the article (1). Patients with early-stage endometrial carcinoma are inherently a low-risk population, but our trial was powered to detect differences in survival consistent with a therapeutic intervention not devoid of important side effects.

The prevalence of lymph node metastases in our trial (ie, 13.3%) was similar to that found in the Mayo Clinic series of patients undergoing systematic pelvic and aortic lymphadenectomy (ie, 14.7%–16%), suggesting that our inclusion criteria were adequate (1,2). Furthermore, pelvic lymphadenectomy failed to play a therapeutic role also in the women with poorly differentiated cancer, who constitute the subgroup with the highest risk of lymph node metastases (1).

In our trial, after a complete pelvic lymphadenectomy, surgeons selected the patients (the majority of whom had grade 3 cancers or bulky or suspicious or positive pelvic and/or aortic lymph nodes) who should receive aortic lymphadenectomy; 26% of the patients in our trial were candidates for this procedure. The rate of isolated aortic metastases or pelvic plus aortic metastases in our trial was in keeping with other reports (3,4), including those from the Mayo Clinic (ie, 2.8% and 7.2%, respectively, in our trial vs 2.8% and 6.7% in Mayo Clinic experience) (1,2). Mariani et al. (2) maintained that the optimal surgical treatment should include systematic lymphadenectomy up to renal vessels in two-thirds of patients with endometrial cancer because “a surgical procedure may be therapeutic if it helps eradicate metastatic disease” and because up to 10% of women could potentially benefit from aortic lymph node dissection.

According to the Gynecologic Oncology Group-33 study (4), patients with aortic lymph node involvement had at least one of the following characteristics: bulky pelvic lymph nodes, macroscopic adnexal metastases, or a grade 3 tumor with outer third myometrial invasion. Mariani et al. did not comment on further intraoperative findings and the clinical assessment of lymph nodes proving to be positive (ie, resection of bulky grossly positive aortic lymph nodes would represent a proper surgical debulking, but with a substantially different oncologic aim). All of these features could be assessed intraoperatively, and a para-aortic lymphadenectomy could be avoided when these features were absent.

Mariani et al. (2) also did not give clinical details about adjuvant therapies and relapses. In our trial, we reported only four relapses at the overall lymph node level in each arm (notably, only one at the aortic level in each arm), whereas most relapses occurred at distant sites (lungs, liver, or bones) (1). We question how an extensive aortic lymph node dissection could actually prevent distant relapses and influence the prognosis.

Three randomized studies and a meta-analysis have shown that external beam radiation therapy given to patients with stage I disease reduced pelvic relapse irrespective of knowing the lymph node status (5), and subgroup analyses of the
Gynecologic Oncology Group-99 trial for intermediate high-risk endometrial cancer (6) showed that the negative lymph node status was not to be considered the only or the most important criterion when deciding to spare external beam radiation therapy.

In conclusion, two randomized trials (1,7) have shown that pelvic lymphadenectomy in patients with clinical early-stage endometrial cancer appears to have no therapeutic role but does improve staging accuracy. We would therefore recommend that more extended lymphadenectomy should not be adopted routinely, that overtreatment should be avoided, and that surgical staging should be tailored to individual patients who frequently have serious comorbidities.

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