



The LACC Trial and Minimally Invasive Surgery in Cervical Cancer

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[Category: Editorial]

### **The LACC Trial and Minimally Invasive Surgery in Cervical Cancer**

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The world was at peace with minimally invasive radical hysterectomy for early cervical cancer until the LACC trial [1] was made public. How can the results be so radically different than previous studies including two meta- analyses? Surgical proficiency should be considered the most important issue of any surgical trial. Randomization is a way to avoid bias in recruiting patients, but it does nothing to compensate for differences in surgical proficiency.

If you accept the results of the LACC trial, it is because you accept that participating surgeons were (a) all competent in the performance of radical hysterectomy and lymphadenectomy, and (b) all equally competent in the laparoscopic as in the open approach.

Gynecologic oncologists realize that the technical nuances of a well performed radical hysterectomy cannot be acquired without subspecialized training. There were participating surgeons who had not completed a fellowship in gynecologic oncology, others were general surgeons with a surgical oncology fellowship, and most had not published their results with laparoscopic radical hysterectomy.

The adequacy of the laparoscopic radical hysterectomy was subjective and based on a review of 2 unedited videos of only type III (not type II, why?), supplied by each surgeon, by the Trial Management Committee. Did each of its 4 members review each one of the videos and was there unanimous agreement? How many videos were submitted but not accepted as adequate because of the lack of radicality? These are unanswered questions.

An important way to objectively assess the radicality of a radical hysterectomy is to measure the length of the removed parametrial tissue [2], a factor also addressed as quality indicator by the international panel who proposed the new classification of radical hysterectomy [3]. However, in the LACC trial, parametrial measurements were not measured. The first 2 authors of the LACC trial [1], however, included parametrial measurements in their study of laparoscopic vs abdominal radical hysterectomy [4]. For these reasons, the LACC trial cannot objectively prove that these were adequately performed laparoscopic radical hysterectomies and that they were performed according to the guidelines described in their addendum [1].

Secondly, we all recognize that learning the laparoscopic approach to radical hysterectomy requires a new set of skills. It is important to remember that the minimally invasive approach for radical hysterectomy did not expand, and probably would have not, until robotic technology was introduced. There were only 45 patients operated by robotics.

In the LACC trial laparoscopic radical hysterectomy included type II and type III and the choice was left to the operating surgeon, since there were no protocol guidelines relative to which type of surgery for which tumor size (without preoperative MRI measurement, which is more accurate than visual estimates), accordingly there are no results provided for each type. We don't know the criteria of each surgeon for each type.

Surgical proficiency may explain other unanswered questions. For instance, the worse outcome of minimally invasive surgery is surprising considering that some surgical quality indicators, with the exception of parametrial measurements, were similar: number of removed and positive lymph nodes, and positive vaginal resection margins. It may also explain why all non-vault pelvic recurrences and more multiple recurrences were observed in the MIS group, and why all recurrences were clustered at 14 of the 33 participating centers. We don't know whether it was because the number of patients entered at each center, the wrong type of radical hysterectomy performed for the tumor size, or the surgeon expertise in laparoscopic radical hysterectomy, or all of above. The exact locations of these recurrences (peritoneal, lymph nodes, port sites other) and the methods used to avoid spread during surgery (use of intra-uterine manipulator, early closure of vagina, and prevention of intraperitoneal spillage) remain unanswered.

It is obvious that this issue cannot be definitely settled until another prospective randomized trial including a single pathologist review, preoperative MRI, parametrial measurements, quality indicators of radical hysterectomy [2, 5], unified criteria for the performance of type B (II) and type C (III) radical hysterectomy, and performance by

gynecologic oncologists with subspecialty board certification or with published results with minimally invasive radical hysterectomy is carried out.

We encourage gynecologic oncologists to critically evaluate the LACC trial and their own experience before deciding to proceed with routine laparotomy for all patients with early cervical cancer. We owe this to our patients with cervical cancer.

### References

1. Ramirez PT, Frumovitz M, Pareja R, et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *N Engl J Med*. 2018;379:1895-1904.
2. Verleye L, Vergote I, Reed N, Ottevanger PB. Quality assurance for radical hysterectomy for cervical cancer: The view of the european organization for research and treatment of cancer--gynecological cancer group (eortc-gcg). *Ann Oncol*. 2009;20:1631-1638.
3. Querleu D, Morrow CP. Classification of radical hysterectomy. *Lancet Oncol*. 2008;9:297-303.
4. Frumovitz M, dos Reis R, Sun CC, et al. Comparison of total laparoscopic and abdominal radical hysterectomy for patients with early-stage cervical cancer. *Obstet Gynecol*. 2007;110:96-102.
5. Bonte AS, Luyckx A, Wyckmans L, Trinh XB, van Dam PA. Quality indicators for the management of endometrial, cervical and ovarian cancer. *Eur J Surg Oncol*. 2018. DOI: 10.2016/j.esjo.2018.10.051.