

 GYNAECOLOGICAL CANCER

Less invasive is not always better

Advances in technology have enabled the introduction of minimally invasive forms of many surgical procedures that were previously conducted using an open approach. The reduced invasiveness of such procedures is, logically, often associated with better perioperative outcomes, although high-quality evidence of long-term oncological non-inferiority can be difficult to obtain.

Now, the findings of a phase III clinical trial and a large registry-based analysis demonstrate that women undergoing minimally invasive radical hysterectomy for early stage cervical cancer have worse progression-free survival (PFS) and overall survival (OS) outcomes than those undergoing more invasive, open radical hysterectomy procedures.

“We initiated this study back in 2008 when we had increasing evidence that minimally invasive surgery was safe in women with endometrial cancer,” explains Pedro Ramirez, the lead author of the phase III trial report, who adds: “We then felt that, before we implemented minimally invasive surgery as the ‘new standard-of-care’ approach for

cervical cancer surgery, we should develop a prospective randomized trial to address not only surgical outcomes but, more importantly, oncological outcomes.”

Both studies demonstrated that women undergoing minimally invasive hysterectomies have inferior outcomes: the trial, in a cohort of 631 patients, revealed 3-year PFS of 91.2% compared with 97.1% among women who underwent open procedures (HR 3.74, 95% CI 1.63–8.58; $P=0.002$), with similar differences in 3-year OS (HR 6.00, 95% CI 1.77–20.30). These conclusions were confirmed in an analysis of registry data from 2,461 women, of whom 49.8% underwent open radical hysterectomy. After a median follow-up duration of 45 months, women undergoing minimally invasive surgery had a 4-year mortality of 9.1% versus 5.3% in women undergoing open surgery who were otherwise matched in terms of baseline characteristics (HR 1.65, 95% CI 1.22–2.22; $P=0.002$).

When asked about the limitations of these studies, Shohreh Shahabi, a co-lead author of the registry analysis, states: “An important

limitation, which applies to both studies, is our inability to explain why minimally invasive surgery was associated with shorter survival.” Ramirez emphasizes “Our study was not designed nor powered to address the question of whether minimally invasive surgery is equivalent to open surgery in the setting of ‘low risk’ cervical cancer.” This aspect remains an unaddressed need.

Shahabi summarizes: “Our findings are consistent with the results of the randomized prospective study of Dr. Ramirez et al. and the National Comprehensive Cancer Network (NCCN) 2019 guidelines have incorporated our evidence. These findings are likely to be practice-changing, with increasing adoption of open surgery in early stage cervical cancer.”

Both investigators highlight the need for thorough patient counselling regarding the real risks associated with open and minimally invasive hysterectomy procedures, on the basis of these new findings. Importantly, the conclusions of these studies emerged despite a plethora of smaller-cohort studies and meta-analyses suggesting oncological equivalence. This scenario highlights the importance of obtaining high-quality evidence, with sufficient follow-up durations, on the effectiveness of new surgical interventions. When asked about future directions, Ramirez states “We are currently preparing a manuscript on the comparison of adverse events between the minimally invasive and open groups in our study,” and Shahabi adds “We are preparing a manuscript on the comparison of the costs, morbidities and mortality related to these surgical approaches.”

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ORIGINAL ARTICLES Ramirez, P. T. et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1806395> (2018) | Melamed, M. et al. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1804923> (2018)



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