

A Randomized Phase III Trial Comparing Radical Hysterectomy and Pelvic Node Dissection (RH) vs Simple Hysterectomy and Pelvic Node Dissection (SH) in Patients with Low-Risk Early-Stage Cervical Cancer (LRESCC). A Gynecologic Cancer Intergroup Study led by Canadian Cancer Trials Group (CCTG CX.5-SHAPE).

Background:

In the last 2 decades, there has been a trend towards less radical surgery in patients with low-risk cervical cancer. Retrospective data suggested that less radical surgery may be safe and associated with less morbidity. The objective of this non-inferiority phase III prospective randomized trial was to compare RH to SH in women with LRESCC.

Methods:

Women with LRESCC defined as FIGO 2018 1A2 or 1B1 disease were randomized to receive RH or SH after stratification by cooperative group, intended use of sentinel node mapping, stage, histological type, and tumour grade. The primary endpoint was pelvic recurrence rate at 3 years (PRR3). Non-inferiority of SH to RH is claimed when the 95% upper one-sided confidence limit (95% UCL) for the difference in PRR3 of SH to RH (DPRR3), calculated by the Kaplan-Meier method for pelvic-relapse free survival, is lower than or equal to 4%. Primary intention to treat (ITT) analysis included all patients randomized. Per-protocol (PP) analysis included eligible patients at baseline and without evidence of more advanced disease found at the time of surgery or final pathology, based on treatment actually received. Secondary endpoints included extrapelvic relapse-free survival (ERFS), overall survival (OS), and quality of life (QoL).

Results:

A total of 700 women were enrolled from December 2012 to November 2019. Patient characteristics were well balanced: median age was 44 (24-80); 91.7% had FIGO stage 1B1 disease and 61.7% had squamous histology. 50% of the hysterectomies were done laparoscopically (56% SH vs. 44% RH), 25% robotically (24% vs. 25%) and 23% abdominally (17% vs. 29%). 4.4% of patients had lymph node metastasis (4.1% in SH and 5.1% in RH) and 3.1% had extrauterine extension (2.6% in SH and 3.7% in RH). A total of 8.8% of women received post-surgical adjuvant therapy (9.2% in SH and 8.4% in RH). With a median follow-up of 4.5 years, 21 pelvic recurrences were identified (11 in SH and 10 in RH group). The PRR3 was 2.5% with SH and 2.2% with RH (DPRR3 0.35% with 95% UCL 2.32%) in ITT analysis; 2.8% with SH and 2.3% with RH (DPRR3 0.42% with 95% UCL 2.56%) in PP analysis. The 3-year ERFS and OS were respectively 98.1% and 99.1% with SH; 99.7% and 99.4% with RH. RH had significantly higher surgery related incidence of urinary incontinence (11.0% vs. 4.7% with SH;  $p=0.003$ ) and urinary retention (9.9% vs. 0.6% with SH;  $p<0.0001$ ) during follow-up. QoL scales with significant difference between the two groups over time were all in favor of SH.

Conclusion:

The pelvic recurrence rate at 3 years in women with low risk early-stage cervical cancer who underwent a simple hysterectomy is not inferior to a radical hysterectomy. Fewer surgical complications and a better quality of life were observed with SH.