Clinicopathologic ChaRacteristics of patients with cervical cAncer having received Simple Hysterectomy (CRASH)

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Surgery for cervical cancer

- Standard surgery for cervical cancer
 - Type 1 hysterectomy for 1A1 LVSI-
 - Type 2 or 3 hysterectomy and lymph node evaluation (LNE) for disease more than 1A1 LVSI-
- Type 1 hysterectomy +- LNE for disease more than 1A1 LVSI-
 - Unexpected cancer
 - Intentional (less radical surgery): SHAPE trial showed type1 hysterectomy is safe in small cancer

Trial Schema Low-risk cervical cancer as defined by: Arm 1 Squamous cell, (Control) adenocarcinoma, Radical adenosquamous carcinoma Hysterectomy* Pelvic Stage IA2 and IB1 < 10 mm stromal recurrence invasion on rate at 3 years LEEP/cone Arm 2 Stratification: < 50% stromal (Experimental) Cooperative Group invasion on MRI Sentinel node mapping (Yes vs No) Max dimension of Simple Stage (IA2 vs IB1) ≤ 20 mm Histological type (Squamous vs Hysterectomy* Grade 1-3 or not adenocarcinoma/adenosquamous) assessable Grade (1-2 vs 3 vs not assessable) *Regardless of treatment assignment, surgery will include pelvic lymph node dissection with optional sentinel lymph node (SN) mapping. If SN mapping is to be done, the mode is optional, but the laparoscopic approach is preferred.

Recurrences

Events	Simple Hysterectomy N=350 (%)	Radical Hysterectomy N=350 (%)	Total N=700 (%)	
Pelvic recurrences	11 (3.1)	10 (2.9)	21 (3.0)	
Vaginal Vault	9 (0.4)	8 (2.3)	17 (2.4)	
Parametrium	1 (0.3)	0	1 (0.1)	
 Pelvic Lymph Nodes 	0	0 0		
• Other	1 (0.3)	2 (0.6)	3 (0.4)	
Extra Pelvic recurrences	7 (2.0)	2 (0.6)	9 (1.3)	
Abdomen	2 (0.6)	0	2 (0.3)	
 Para-aortic lymph nodes 	2 (0.6)	2 (0.6)	4 (0.6)	
Supraclavicular L N	1 (0.3)	0	1 (0.1)	
Other	2 (0.6)	0	2 (0.3)	
Pelvic and extra pelvic recurrences	3 (0.9)	2 (0.6)	5 (0.7)	
Extra pelvic only recurrences	4 (1.1)	0	4 (0.6)	
Pelvic or extra pelvic recurrences	15 (4.3)	10 (2.9)	25 (3.6)	















Adjuvant therapy after surgery

- After type 2 or 3 hysterectomy
 - High risk factors (ANY of lymph node, parametrium or margin)
 - Intermediate risk factors (Sedlis criteria): combination of tumor size, invasion depth and LVSI
- After type 1 hysterectomy for small tumor
 - Not well studied
 - May be over-treated: 31% adjuvant therapy rate in systematic review [PMID: 33306971]
 - NCCN guideline: Same to criteria after type 2 or 3 hysterectomy
 - Incidental cervical cancer section "No definitive data are available to guide the appropriate adjuvant treatment of these patients"
 - GOG 278: High risk factors OR deep invasion (>10mm)
 - SHAPE: As per local center policy. Adjuvant therapy in 8-9% (LN+ 3-4%, parametrium 0-2%, margin 2-3%)
- Lack of data guiding the appropriate adjuvant therapy after type 1 hysterectomy

Objective and Study design

- Examine the recurrence pattern in women with cervical cancer who received type 1 hysterectomy to guide the appropriate adjuvant therapy after type 1 hysterectomy
- Retrospective study

Eligibility criteria

Inclusion

- Histologically confirmed, newly diagnosed cervical cancer
- Squamous cell carcinoma or adenosquamous cell carcinoma or adenocarcinoma
- Type 1 hysterectomy +- LNE was performed

Exclusion

- Stage 1A1 and LVSI negative
- High risk factors present (lymph node metastasis, parametrium involvement, and resection margin involvement)
- Preoperative chemotherapy or radiotherapy
- Gross residual tumor exist after type 1 hysterectomy
- Other cancer diagnosed

Variables

- Demographics
- Conization
- Type 1 hysterectomy +- LNE
- Adjuvant therapy
- Follow up, recurrence
 - Tumor size, invasion depth and LVSI will be estimated using both conization and type 1 hysterectomy data

Analysis

Subgroup	Tumor size	Invasion depth	LVSI	LN surgically evaluated rate	Adjuvant therapy rate	PFS curve
1	<=1cm	<= 1/2	-			
2	<=1cm	<= 1/2	+			
3	<=1cm	> 1/2	-			
4	<=1cm	> 1/2	+			
5	>1cm AND <= 2cm	<= 1/2	-			
6	>1cm AND <= 2cm	<= 1/2	+			
7	>1cm AND <= 2cm	> 1/2	-			
8	>1cm AND <= 2cm	> 1/2	+			
9	> 2cm	<= 1/2	-			
10	> 2cm	<= 1/2	+			
11	> 2cm	> 1/2	-			
12	> 2cm	> 1/2	+			

^{*}Merge subgroups with similar outcomes (adjuvant rate, PFS) into a bigger group

Plan

- 2023 4Q Study initiation at KGOG
- 2024 1Q International group participation
- 2024 3Q International group data collection initiation
- 2025 2Q Data collection completion
- 2025 4Q Analysis
- N = 500