

The Prognostic Values of HPV Genotypes and Tumor PD-L1 Expression in Patients With HPV-associated Endocervical Adenocarcinoma

Zhou F, Chen H, Li M, et al.
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要旨

High-risk HPV, hrHPV は子宮頸部腺癌の発生に関与するが、hrHPV subtype が予後および他の予後予測因子変数との関連性するかは不明である。

筆者らは、hrHPV subtype に基づき子宮頸部 HPV 関連腺癌 HPV-associated cervical adenocarcinoma, HPVACA 120 症例を 3 群 (HPV16+, HPV18/45+, およびその他の subtype+) に分類し、hrHPV subtype と進行期、浸潤パターン (Silva)、および PD-L1 発現状態との関係を検討した。

120 例中 51 例 (42.5%) は HPV16 群、50 例 (41.7%) は HPV18 または 18/45 群、9 例 (7.5%) が他の hrHPV subtype 群であった。hrHPV subtype 群間で進行期 (P=0.51)、浸潤パターン (P=0.55)、および PFS (P=0.59) に有意差はみられなかった。HPVACA では PD-L1 陽性例は比較的多くみられた (腫瘍割合スコア, TPS で 25%、複合陽性スコア, CPS で 55%)。TPS では、HPV16 群の 19.6% (10/51)、HPV18/45 群の 32.0% (16/50)、およびその他の subtype 群の 22.2% (2/9) で PD-L1 陽性であったが、3 群間で PD-L1 発現に有意な違いはみられなかった (P=0.35)。

Silva pattern B および C 症例における PD-L1 陽性群は、Silva pattern A 例も有意に高かった (P=0.00002)。CPS または TPS のいずれかによる PD-L1 陽性例は、PD-L1 陰性例よりも PFS は有意に短縮した (CPS, P=0.025; TPS, P=0.001)。

Take Home Message

1. hrHPV subtype と HPVACA の予後および予後予測因子の間に相関はない。
2. PD-L1 の発現は HPVACA において陰性予後マーカーとして機能する。

TABLE 1. Clinicopathologic Information of Patients With HPV A ECA

Genotype Groups	Age, Median (Range)	Test Modules, n (%)			FIGO Stages, n (%)				Follow-up, n (%)			Total
		AHPV	Cobas	HC2	I	II-IV	NA	P	R	M	D	
16	47 (28-67)	37 (73)	14 (27)	0	41 (80)	4 (8)	6 (12)	0.51	2 (4)	2 (4)	0	51
18	45 (27-62)	34 (68)	16 (32)	0	38 (76)	5 (10)	7 (14)		3 (6)	0	2 (4)	50
O	58 (45-73)	9 (100)	0	0	7 (78)	2 (22)	0		0	0	0	9
16 or 18+	47 (37-57)	0	0	10 (100)	10	0	0	NA	0	0	0	10
Total												120

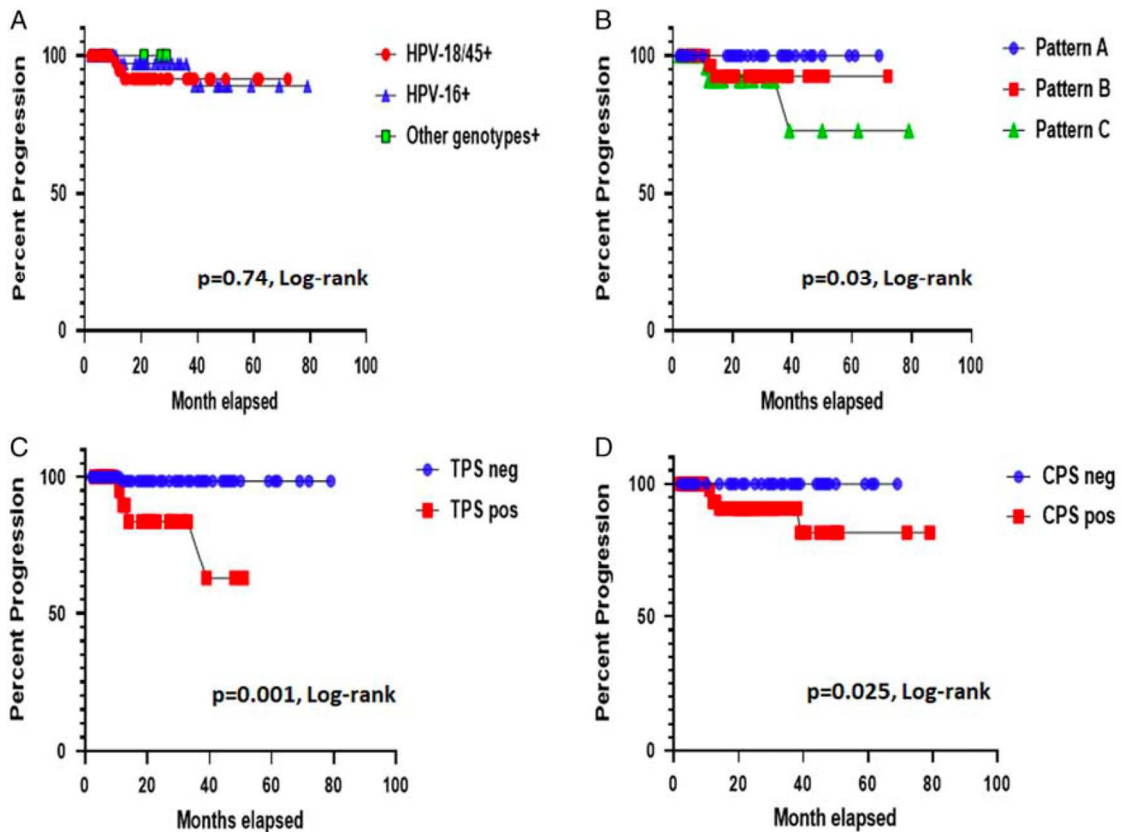
16 indicates HPV16+; 18, HPV18 or 18/45+; D, death; M, metastasis; NA, not available; O, other HPV genotypes+; R, recurrence.

TABLE 2. PD-L1 Expression in HPV A ECA in Various HPV Genotype Groups

HPV Genotype Groups	Invasion Patterns, n (%)			PD-L1 Expression, n (%)				Total
	A	B	C	TPS		CPS		
				+	-	+	-	
16	20 (39)	18 (35)	13 (26)	10 (20)	41 (80)	24 (47)	27 (53)	51
18	16 (32)	16 (32)	18 (36)	16 (32)	34 (68)	32 (64)	18 (36)	50
O	4 (40)	4 (40)	2 (20)	2 (22)	7 (78)	7 (78)	2 (22)	9
16 or 18+ (HC2 test)	3 (33)	2 (22)	4 (44)	2 (20)	8 (80)	3 (30)	7 (70)	10
Total								120
P	0.51 (16 vs. 18); 0.55 (across groups)			0.15 (16 vs. 18); 0.35 (across groups)		0.11 (16 vs. 18); 0.10 (across groups)		

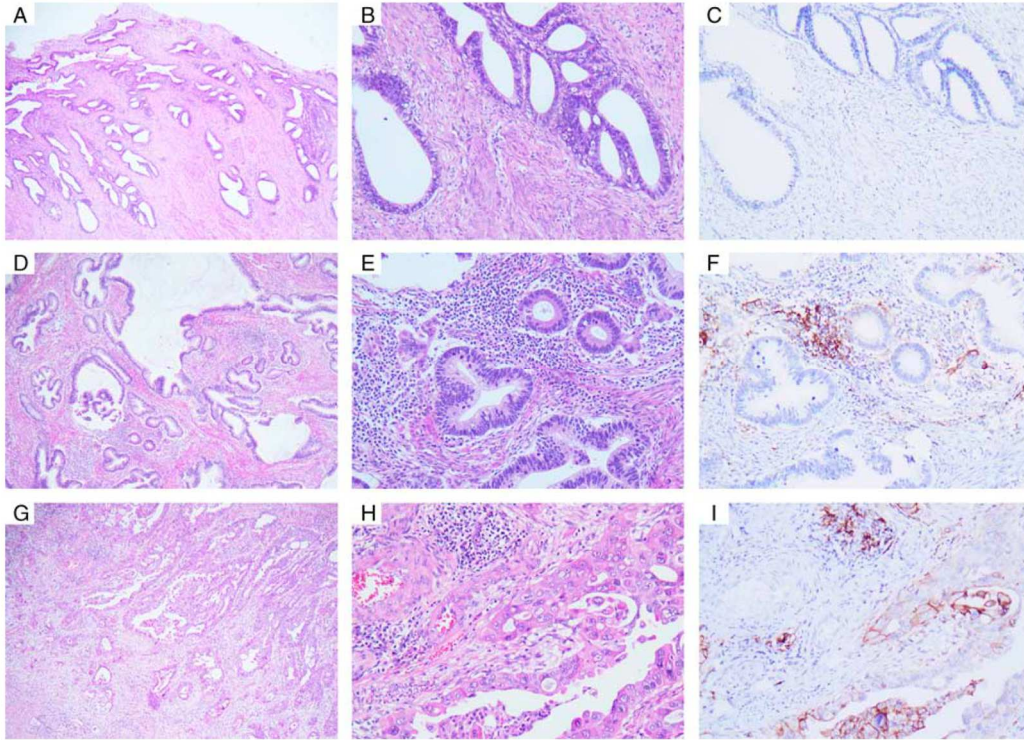
16 indicates HPV16+; 18, HPV18 or 18/45+; O, other HPV genotypes+.

Fig. 1



Kaplan-Meier curves of PFS in patients with HPV A ECA. A, PFS in patients with HPV A ECA from different HPV genotype groups (red circle: group 18; blue triangle: group 16; green square: group O). B, PFS in patients with HPV A ECA with 3 different invasion patterns (blue circle: pattern A tumors; red square: pattern B tumors; green triangle: pattern C tumors). C, PFS in PD-L1-positive group (red) and PD-L1-negative group (blue) using TPS (cutoff 1%). D, PFS in PD-L1-positive group (red) and PD-L1-negative group (blue) using CPS (cutoff 1).

Fig. 2



Examples of HPV-associated endocervical adenocarcinoma (ECA) with different patterns of invasion and corresponding PD-L1 immunostain. A–C, Pattern A tumor. A, Hematoxylin and eosin (H&E) at low magnification shows well-formed glands with smooth contours and absence of destructive-type invasion or stromal desmoplasia. B, Malignant glands with rounded contours and absence of destructive invasion at medium power (H&E). C, Corresponding negative PD-L1. D–F, Pattern B tumor with corresponding PD-L1. D, Predominantly rounded glands with a few foci of early destructive-type invasion and desmoplastic stromal response (H&E). E, A gland with a focus of early destructive invasion, stromal desmoplasia and adjacent inflammatory infiltrate from the same case (H&E). F, Corresponding PD-L1 showing expression in both tumor cells and immune cells. G–I, Pattern C tumor with corresponding PD-L1. G, Invasive tumor with diffusely destructive invasion pattern (H&E). H, Irregularly shaped, angulated glands with destructive-type invasion (H&E). I, Corresponding PD-L1 with high expression in both tumor cells and immune cells.

TABLE 3. PD-L1 Expression in ECA With Various Invasion Patterns

Diagnosis	PD-L1 Expression, n (%)				Total
	TPS		CPS		
	+	-	+	-	
Pattern A	1 (2.3)	42 (97.7)	8 (18.6)	35 (81.4)	43
Pattern B	13 (32.5)	27 (67.5)	31 (77.5)	9 (22.5)	40
Pattern C	16 (43.2)	21 (56.8)	28 (75.7)	9 (24.3)	37
Total					120
<i>P</i>	0.0002 (A vs. B); <0.0001 (A vs. C); 0.00002 (A vs. B+C); 0.33 (B vs. C)		<0.00001 (A vs. B); <0.0001 (A vs. C); <0.00001 (A vs. B+C); 0.85 (B vs. C)		