

Risk Factors for Heterotopic Ossification Following Multiligament Knee Injury

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Background

- Heterotopic ossification (HO) is the atypical formation of bone in extraskelatal tissues that can occur after localized trauma, after neurological injury, or as a post-surgical complication, and can result in significant pain, ROM deficits and mechanical block that may necessitate surgical excision.
- HO develops in 21-43% of patients following multiple ligament knee injury (MLKI), making it one of the most common postoperative complications in this population. However, risk factors remain poorly understood.
- Thus, the primary aim of this study was to investigate (1) the risk factors for HO following MLKI, and (2) the regions of the knee that are most susceptible to HO following MLKI.**

Methods

- Inclusion Criteria:** Patients treated for an MLKI by a single surgeon at a Level 1 trauma center between 2001 and 2023, with initial X-rays at the time of injury and X-rays at a minimum of 6 months follow-up.
- Radiographic Review:** Two senior musculoskeletal radiologists reviewed all patients for presence of HO in the most recent radiograph using the initial x-rays obtained at the time of injury for comparison.
- Statistical Analysis:** Odds ratios (OR) for HO were assessed using multivariable logistic regression, adjusted for ligament injury classification, MOI, documented dislocation, central nervous system (CNS) trauma, and knee-spanning external fixation.

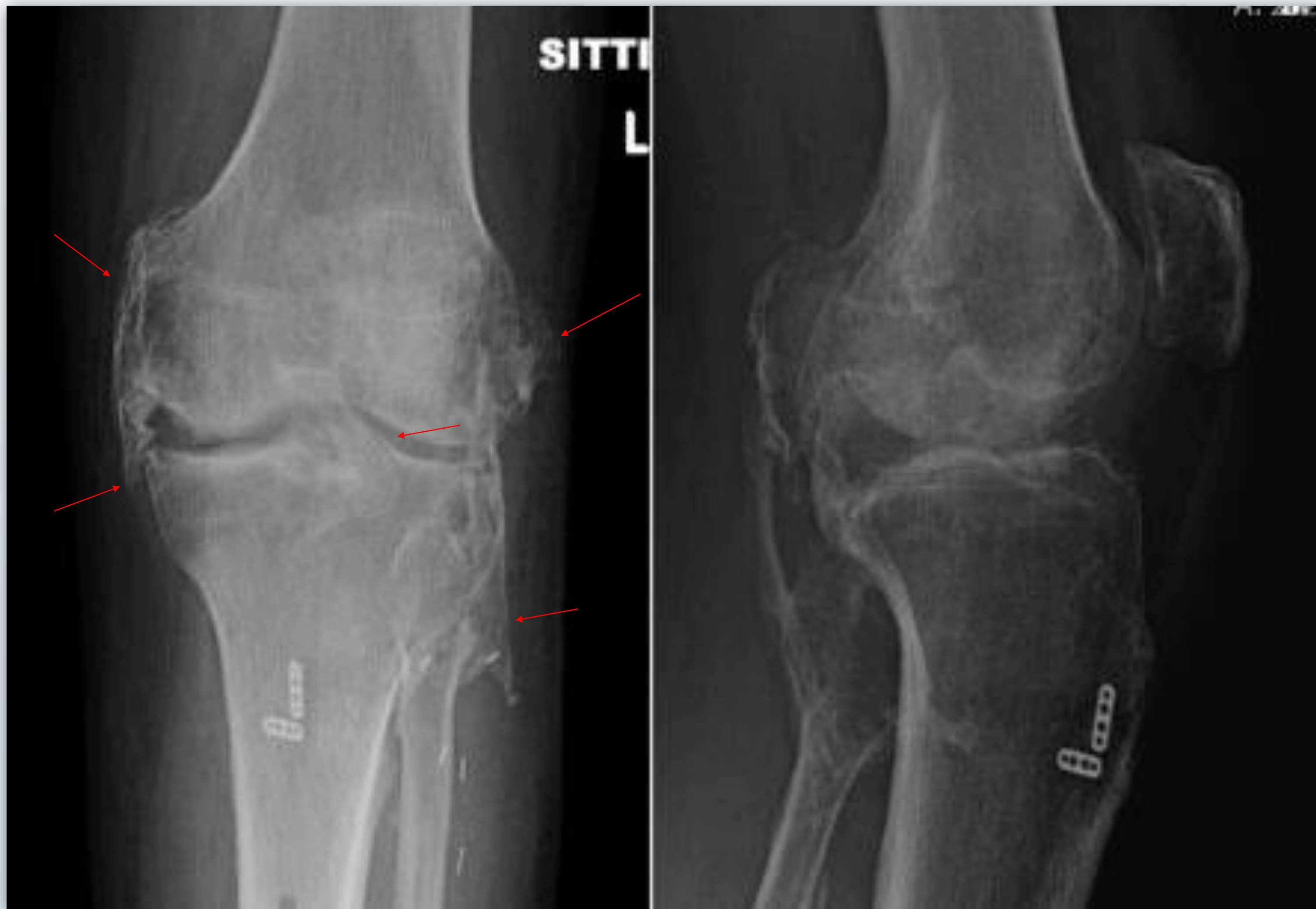


Figure 1. Heterotopic ossification on radiographs following a KD4 injury

Results

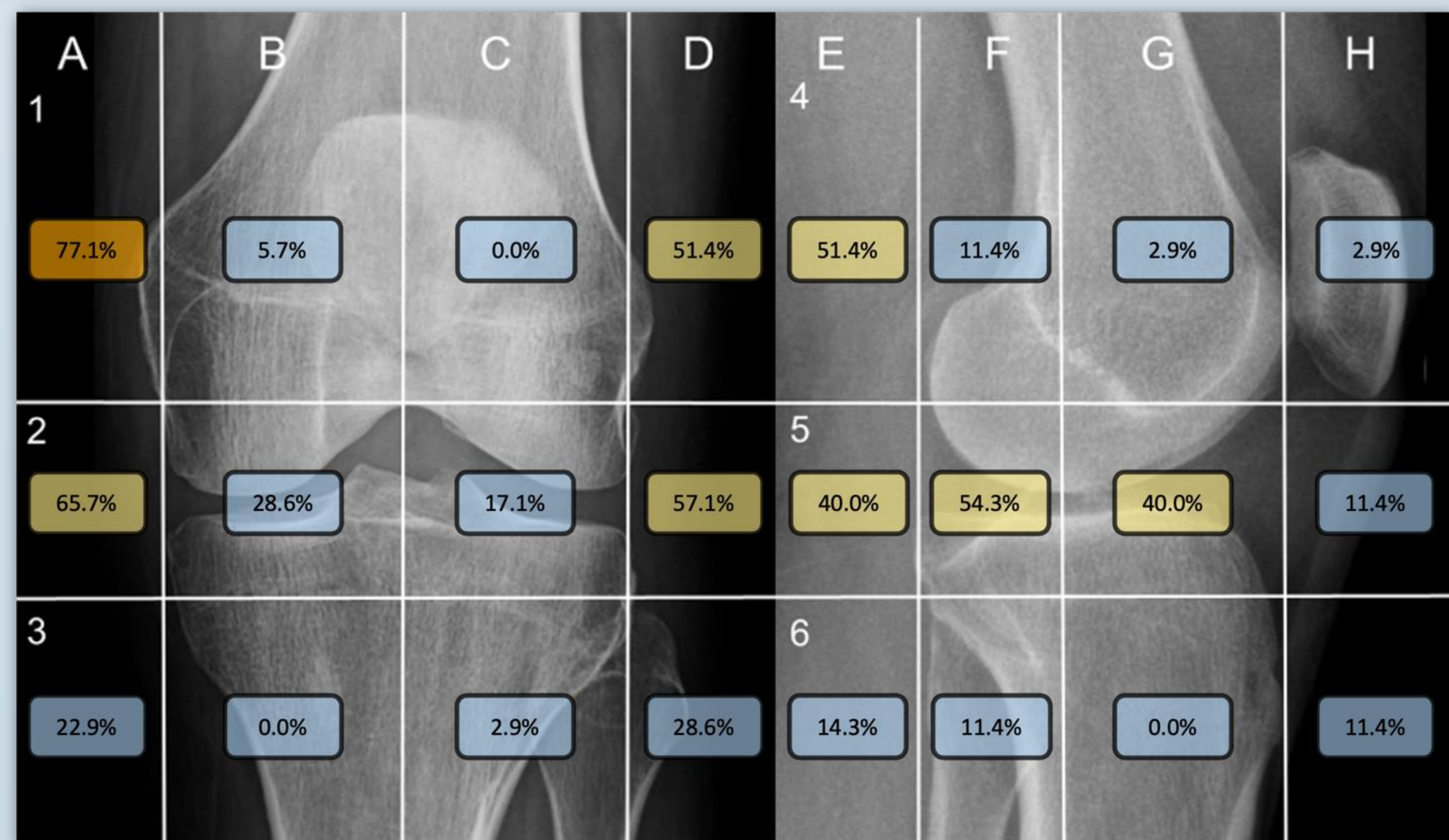


Figure 2. Frequency of HO development by knee location

Results

Table 1. Univariable Analysis of Risk Factors for HO

Variable	Total (N = 100)	No HO (N = 65)	HO (N = 35)	Odds Ratio (95% CI)	P-value
Age (year), mean ± SD	35.5 ± 13.6	34.2 ± 14.1	38 ± 12.5	1.02 (0.99-1.05)	0.19
Sex					0.49
Female	27 (27.0%)	19 (29.2%)	8 (22.9%)	0.72 (0.28-1.86)	
Male	73 (73.0%)	46 (70.8%)	27 (77.1%)		
Ligament Injury Classification†					0.045
KDI or MLKI-1	17 (17.0%)	14 (21.5%)	3 (8.6%)		
KDII or MLKI-2	3 (3.0%)	1 (1.5%)	2 (5.7%)		
KDIII or MLKI-3	40 (40.0%)	24 (36.9%)	16 (45.7%)		
KDIIIM or MLKI-3M	10 (25.0%)	4 (16.7%)	6 (37.5%)		
KDIIIL or MLKI-3L	30 (75.0%)	20 (83.3%)	10 (62.5%)		
KDIV or MLKI-4	14 (14.0%)	6 (9.2%)	8 (22.9%)		
KDV	26 (26.0%)	20 (30.8%)	6 (17.1%)		
KDV.1	4 (15.4%)	4 (20.0%)	0 (0.0%)		
KDV.3L	13 (50.0%)	11 (55.0%)	2 (33.3%)		
KDV.3M	5 (19.2%)	2 (10.0%)	3 (50.0%)		
KDV.4	4 (15.4%)	3 (15.0%)	1 (16.7%)		
Mechanism of Injury					0.06
Ultralow velocity	4 (4.0%)	1 (1.5%)	3 (8.6%)	4.39 (0.33-243.2)	
Low energy	41 (41.0%)	31 (47.7%)	10 (28.6%)	0.49 (0.18-1.28)	
High energy	55 (55.0%)	33 (50.8%)	22 (62.9%)	Reference	
Documented dislocation					0.032
Yes	40 (40.0%)	21 (32.3%)	19 (54.3%)	2.49 (1.07-5.79)	
No	60 (60.0%)	44 (67.7%)	16 (45.7%)		
Peroneal nerve injury					0.83
Yes	27 (27.0%)	18 (27.7%)	9 (25.7%)	0.90 (0.36-2.30)	
No	73 (73.0%)	47 (72.3%)	26 (74.3%)		
Vascular injury					0.09
Yes	10 (10.0%)	4 (6.2%)	6 (17.1%)	3.16 (0.83-12.05)	
No	90 (90.0%)	61 (93.8%)	29 (82.9%)		
CNS Trauma					0.005
Yes	17 (17.0%)	6 (9.2%)	11 (31.4%)	4.51 (1.50-13.57)	
No	83 (83.0%)	59 (90.8%)	24 (68.6%)		
Knee-Spanning External Fixation					<0.001
Yes	27 (27.0%)	9 (13.8%)	18 (51.4%)	6.59 (2.51-17.33)	
No	73 (73.0%)	56 (86.2%)	17 (48.6%)		
PCL reconstruction					0.187
Yes	91 (91.0%)	61 (93.8%)	30 (85.7%)	2.542 (0.636-10.159)	
No	9 (9.0%)	4 (6.2%)	5 (14.3%)		
ACL reconstruction					0.135
Yes	87 (87.0%)	59 (90.8%)	28 (80%)	2.458 (0.756-7.997)	
No	13 (13.0%)	6 (9.2%)	7 (20.0%)		
Arthroscopic Surgery					0.660
Yes	40 (40.0%)	25 (38.5%)	15 (42.9%)	1.20 (0.520-2.777)	
No	60 (60.0%)	40 (61.5%)	20 (57.1%)		
Open Surgery					0.111
Yes	83 (83.0%)	51 (78.5%)	32 (91.4%)	2.92 (0.78-10.99)	
No	17 (17.0%)	14 (21.5%)	3 (8.6%)		
Time to 1 st surgery	85.65 ± 254.84	92.23 ± 220.72	74.97 ± 305.82	1.000 (0.998-1.002)	0.782

Table 3. Univariable Analysis of Soft Tissue Injury Patterns Based on HO Status

Variable	Injury Status	HO (N = 35)	No HO (N = 65)	Total (N = 100)	P-value
ACL Tear	Yes	33 (94.3%)	56 (86.2%)	89 (89.0%)	0.32
	No	2 (5.7%)	9 (13.8%)	11 (11.0%)	
Partial tear	Yes	1 (2.9%)	9 (13.8%)	10 (10.0%)	
	No	34 (97.1%)	56 (86.2%)	90 (90.0%)	
Femoral avulsion	Yes	2 (5.7%)	2 (3.1%)	4 (4.0%)	0.19
	No	33 (94.3%)	63 (96.9%)	96 (96.0%)	
Midsubstance tear	Yes	24 (68.6%)	39 (60.0%)	63 (63.0%)	
	No	11 (31.4%)	26 (40.0%)	37 (37.0%)	
Tibial avulsion	Yes	6 (17.1%)	6 (9.2%)	12 (12.0%)	
	No	29 (82.9%)	59 (90.8%)	88 (88.0%)	
PCL tear	Yes	34 (97.1%)	56 (86.2%)	90 (90.0%)	0.16
	No	1 (2.9%)	9 (13.8%)	10 (10.0%)	
Partial tear	Yes	5 (14.3%)	9 (13.8%)	14 (14.0%)	
	No	30 (85.7%)	56 (86.2%)	86 (86.0%)	
Femoral avulsion	Yes	8 (22.9%)	9 (13.8%)	17 (17.0%)	
	No	27 (77.1%)	56 (86.2%)	83 (83.0%)	0.26
Midsubstance tear	Yes	15 (42.9%)	32 (49.2%)	47 (47.0%)	
	No	20 (57.1%)	33 (50.8%)	53 (53.0%)	
Tibial avulsion	Yes	6 (17.1%)	6 (9.2%)	12 (12.0%)	
	No	29 (82.9%)	59 (90.8%)	88 (88.0%)	
MCL tear	Yes	19 (54.3%)	23 (35.4%)	42 (42.0%)	0.07
	No	16 (45.7%)	42 (64.6%)	58 (58.0%)	
Partial tear	Yes	2 (5.7%)	8 (12.3%)	10 (10.0%)	
	No	33 (94.3%)	57 (87.7%)	90 (90.0%)	
Femoral avulsion	Yes	9 (25.7%)	6 (9.2%)	15 (15.0%)	
	No	26 (74.3%)	59 (90.8%)	85 (85.0%)	0.06
Midsubstance tear	Yes	6 (17.1%)	4 (6.2%)	10 (10.0%)	
	No	29 (82.9%)	61 (93.8%)	90 (90.0%)	
Tibial avulsion	Yes	2 (5.7%)	5 (7.7%)	7 (7.0%)	
	No	33 (94.3%)	60 (92.3%)	93 (93.0%)	
LCL tear	Yes	22 (62.9%)	52 (80.0%)	74 (74.0%)	0.06
	No	13 (37.1%)	13 (20.0%)	26 (26.0%)	
Partial tear	Yes	1 (2.9%)	6 (9.2%)	7 (7.0%)	
	No	34 (97.1%)	59 (90.8%)	93 (93.0%)	
Femoral avulsion	Yes	7 (20.0%)	12 (18.5%)	19 (19.0%)	
	No	28 (80.0%)	53 (81.5%)	81 (81.0%)	0.37
Midsubstance tear	Yes	2 (5.7%)	5 (7.7%)	7 (7.0%)	
	No	33 (94.3%)	60 (92.3%)	93 (93.0%)	
Fibular avulsion	Yes	12 (34.3%)	29 (44.6%)	41 (41.0%)	
	No	23 (65.7%)	36 (55.4%)	59 (59.0%)	
POL tear	Yes	9 (25.7%)	4 (6.2%)	13 (13.0%)	0.006
	No	26 (74.3%)	61 (93.8%)	87 (87.0%)	
Popliteus tendon tear	Yes	20 (57.1%)	41 (63.1%)	61 (61.0%)	0.56
	No	15 (42.9%)	24 (36.9%)	39 (39.0%)	
IT band avulsion or tear	Yes	9 (25.7%)	14 (21.5%)	23 (23.0%)	0.64
	No	26 (74.3%)	51 (78.5%)	77 (77.0%)	
Biceps Femoris tear	Yes	17 (48.6%)	34 (52.3%)	51 (51.0%)	
	No	18 (51.4%)	31 (47.7%)	49 (49.0%)	0.72
PFL tear	Yes	7 (20.0%)	24 (36.9%)	31 (31.0%)	0.08
	No	28 (80.0%)	41 (63.1%)	69 (69.0%)	
Patellar tendon tear	Yes	4 (11.4%)	7 (10.8%)	11 (11.0%)	1.00
	No	31 (88.6%)	58 (89.2%)	89 (89.0%)	
MPFL tear	Yes	12 (34.3%)	12 (18.5%)	24 (24.0%)	0.08
	No	23 (65.7%)	53 (81.5%)	76 (76.0%)	

Note: POL = Posterior oblique ligament; PFL = Popliteofibular ligament; MPFL = medial patellofemoral ligament

Table 4. Multivariable Analysis of Risk Factors for HO

Variable	Adjusted OR	95% CI	p-value
Knee-Spanning External Fixation	8.51	2.281-31.717	0.001
Central Nervous System Trauma	6.63	1.507-29.209	0.012
Documented Dislocation	1.06	0.324-3.444	0.927
Ligamentous Injury Classification	-	-	0.513
Mechanism of Injury	-	-	0.580

Reference Group: No HO

Conclusions

- In patients sustaining MLKI, knee-spanning external fixation and CNS trauma were independently associated with HO, whereas ligament injury classification, MOI, and documented dislocation were not. The overall incidence of HO after MLKI in our cohort was 35%, most commonly in the posterior, medial, and proximal knee regions. Future studies with larger cohorts are necessary to accurately decipher the unique contributions of various patient characteristics, injury patterns, and surgical interventions on the development of HO following MLKI.