

Background & Objectives

❖ Background

- Bone fracture is a devastating event in patients with metastatic colorectal cancer (mCRC).
- To date, no study has compared osteoporotic fracture (OF) and pathologic fracture (PF) in mCRC patients.

❖ Objectives

- This study aimed to compare the incidence rate of OF and PF in patients with mCRC who received palliative chemotherapy, and to identify risk factors for OF.

Methods

❖ Study design

- A retrospective cohort study using the clinical data warehouse of Seoul National University Bundang Hospital in Korea
- OF was defined as fractures caused by low-energy trauma occurring at any site excluding skull, face, hands, ankles, and feet.

❖ Study population

- Patients with mCRC who received palliative chemotherapy from January 2009 to December 2015
- Patients who did not receive irinotecan- or oxaliplatin-based doublet or triplet chemotherapy were excluded.

❖ Primary outcome

- Cumulative incidence of the first OF and PF

❖ Secondary outcome

- Incidence rate of the OF and PF
- Risk factors for OF

❖ Statistical analysis

- Kaplan-Meier method
- Cox proportional hazard model
- Fine-Gray model (Subdistribution hazard ratio, SDHR)
- Analyses were conducted using R software, version 4.2.2.

Results

Table 1. Baseline characteristics of the study patients (n = 622)

Variable	Value
Age (years), median (range)	61.0 (20.0-91.0)
Sex, n (%)	
Male	359 (57.7)
Body mass index (kg/m ²), median (range)	22.6 (13.8-36.2)
Primary tumor location	
Right	163 (26.2)
Left	458 (73.6)
Initially metastatic/Recurrent disease, n (%)	
Recurrent	160 (25.7)
Initially metastatic	462 (74.3)
Bone metastasis (Yes), n (%)	42 (6.8)
1st Chemotherapy	
Oxaliplatin	313 (50.3)
Irinotecan	309 (49.7)
Target agents	
Cetuximab	71 (11.4)
Bevacizumab	195 (31.4)
ECOG performance status	
0-1	571 (91.8)
2	41 (6.6)
Comorbidity	
Diabetes mellitus	133 (21.4)
Osteoporosis	34 (5.5)
Prevalent fracture (Yes), n(%)	59 (9.5)
GFR (mL/min/1.73m ²), median (range)	97.0 (11.1-286.2)
Albumin (g/dL), median (range)	3.9 (0.6-6.5)
Corrected Ca (mg/dL), median (range)	8.8 (6.2-11.8)

Table 3. Risk of the first OF

Variable	Group	Univariate analysis			Multivariate analysis [†]			Fine-Gray model analysis [†]		
		HR	95% CI	P-value	HR	95% CI	P-value	SDHR	95% CI	P-value
Age (N=622)	Continuous	1.06	1.03-1.09	<0.001	1.04	1.01-1.08	0.004	1.04	1.01-1.08	0.010
Sex (N=622)	Male	1								
	Female	1.19	0.66-2.12	0.565						
Body mass index (kg/m ²) (N=614)	< 18.5	1								
	18.5-22.9	0.48	0.16-1.49	0.205						
	≥ 23	1.07	0.37-3.04	0.907						
Primary Tumor location (N=621)	Right	1			1			1		
	Left	0.54	0.29-0.99	0.045	0.64	0.34-1.19	0.155	0.60	0.32-1.11	0.100
Initially metastatic vs recurrent (N=622)	Recurrent	1								
	Initially metastatic	1.21	0.62-2.34	0.579						
Bone metastasis (N=622)	No	1								
	Yes	2.13	0.65-7.00	0.213						
1st Chemotherapy (N=622)	Oxaliplatin	1								
	Irinotecan	0.79	0.44-1.42	0.427						
Target agents (N=622)	Not used	1								
	Cetuximab	1.59	0.72-3.49	0.250						
	Bevacizumab	0.71	0.34-1.46	0.352						
ECOG performance status (N=612)	0-1	1								
	2	2.04	0.73-5.72	0.174						
Diabetes mellitus (N=622)	No	1								
	Yes	1.39	0.73-2.64	0.318						
Osteoporosis (N=622)	No	1			1			1		
	Yes	7.37	3.73-14.56	<0.001	3.80	1.76-8.22	<0.001	3.29	1.24-8.73	0.017
Prevalent fracture (N=622)	No	1			1			1		
	Yes	3.05	1.47-6.34	0.003	1.54	0.70-3.38	0.284	1.63	0.63-4.21	0.310
GFR (mL/min/1.73m ²) (N=615)	≥ 60	1								
	< 60	2.45	0.96-6.21	0.060						
Albumin (g/dL) (N=615)	≥ 3.3	1								
	< 3.3	1.10	0.34-3.57	0.877						
Corrected Ca (mg/dL) (N=615)	≥ 8.8	1								
	< 8.8	0.93	0.52-1.67	0.805						

[†] Multivariate and Fine-Gray model were analyzed with the variables that were significant in the univariate analysis.

Table 2. The incidence rate of the first OF and PF

	Osteoporotic fracture	Pathologic fracture
Incidence rate (95% CI) (case/ 100 person-year)	2.29 (1.68-3.05)	1.95 (1.39-2.65)
Fracture site [†] (N, % of total fracture cases)		
Lumbar spine	22 (47.8)	12 (30.0)
Thoracic spine	9 (19.6)	18 (45.0)
Cervical spine	0 (0)	3 (7.5)
Pelvis, hip	2 (4.3)	4 (10.0)
Femur	4 (8.7)	4 (10.0)
Forearm, wrist	2 (4.3)	0 (0)
Humerus, shoulder	0 (0)	2 (5.0)
Ankle, lower leg	1 (2.2)	0 (0)
Rib	11 (23.9)	2 (5.0)

[†] OF and PF were observed in 46 and 40 patients, respectively. The total percentage may exceed 100% because some patients have fractures in multiple sites concurrently. The most common fracture sites were the lumbar spines (47.8%) followed by rib (23.9%) in OF and the thoracic spines (45.0%) followed by lumbar spine (30.0%) in PF, respectively.

Results (cont'd)

- In the total of 622 patients, the median age and BMI were 61 years and 22.6 kg/m², respectively. Bone metastasis was found in 42 patients (6.8%). During a median follow-up of 3.2 (range 0.02-12.94) years, the cumulative incidence rate of the first OF and PF was 4.5% and 4.2% at 2 years. In the patients aged 70 or older, the cumulative incidence rate of the first OF was 5.5% and 8.0% at 1 year and at 2 years, respectively.

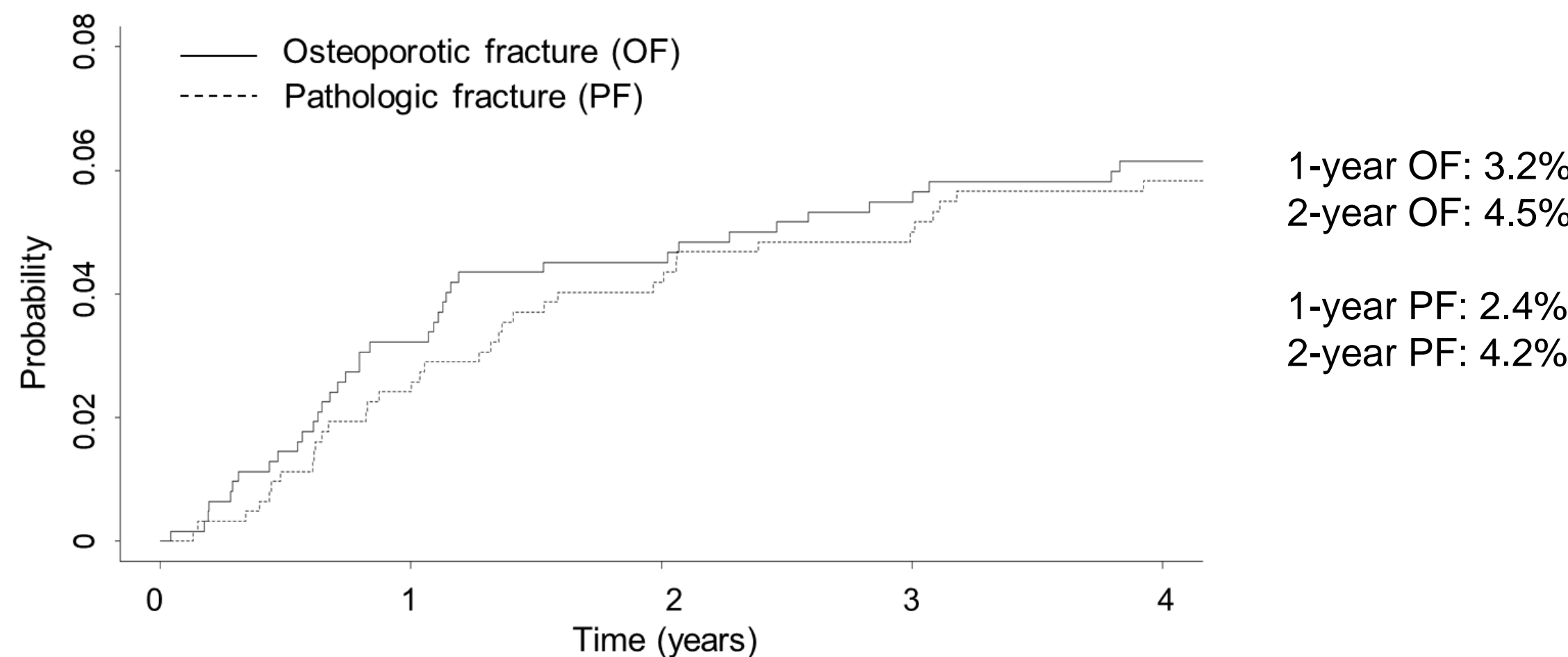


Figure 1. Cumulative incidence of OF and PF in total study population

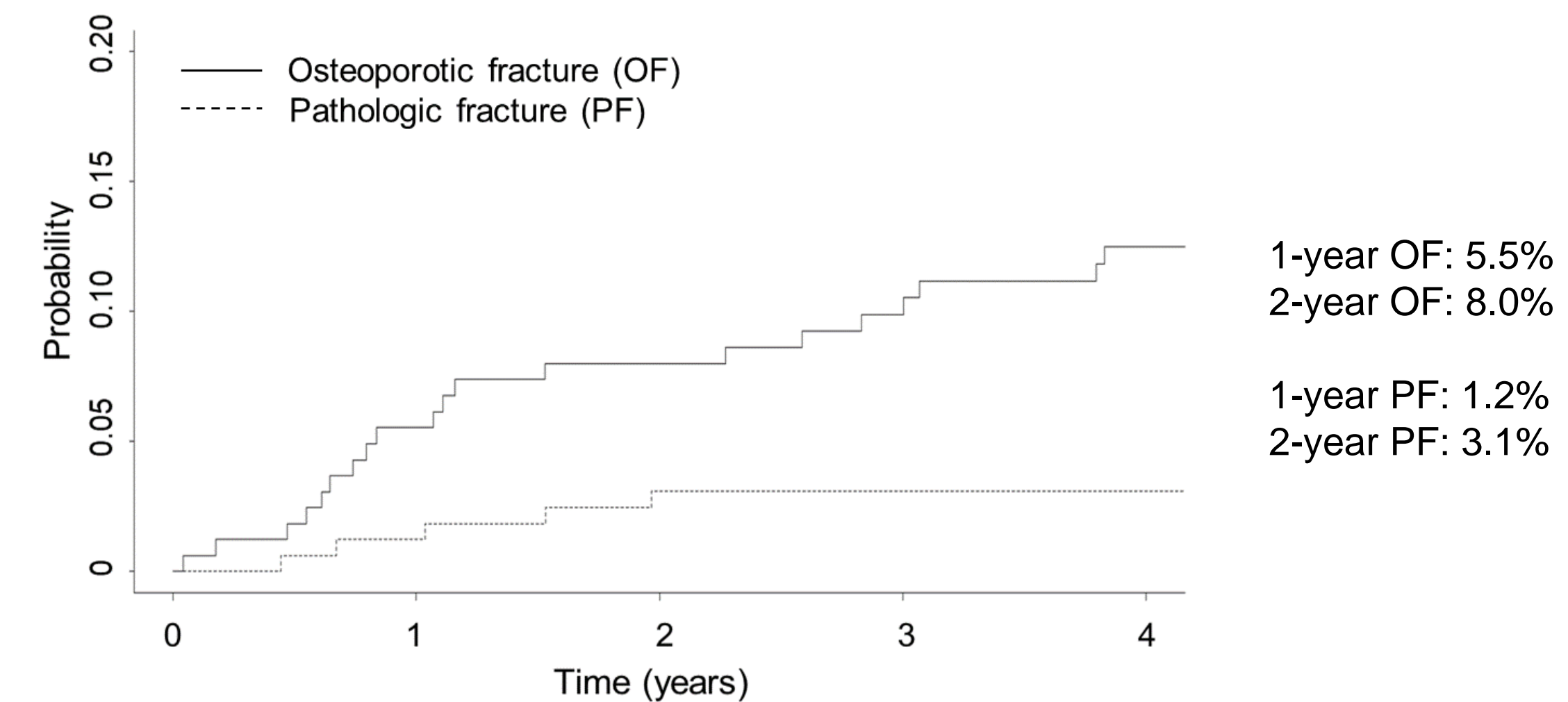


Figure 2. Cumulative incidence of OF and PF in patients ≥ 70 years

Conclusions

- Significant OFs were observed in patients with mCRC who received palliative chemotherapy, with the most frequent location being in the lumbar spine.
- Age and osteoporosis history were significant risk factors for OF.
- The OF risk should be considered in patients with mCRC receiving palliative chemotherapy, especially in the elderly or those with osteoporosis history.