

Preoperative systemic inflammation in pelvic chondrosarcoma: prognostic associations and limited incremental value beyond clinicopathological factors

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Abstract

Background

The prognostic contribution of preoperative inflammatory markers in pelvic chondrosarcoma remains uncertain. We evaluated the modified Glasgow Prognostic Score (mGPS), C-reactive protein-to-albumin ratio (CAR), and neutrophil-to-lymphocyte ratio (NLR).

Methods

This single-centre retrospective cohort included 110 patients who underwent definitive surgery for primary pelvic chondrosarcoma between 2014 and 2021. Blood samples were obtained within 14 days before surgery. Overall survival (OS) was the primary outcome; distant metastasis and local recurrence were secondary outcomes. Each inflammatory marker was added separately to a prespecified clinicopathological Cox model. Competing-risk cumulative incidence was used for distant metastasis and local recurrence, with death treated as a competing event.

Results

Median follow-up was 87.5 months; 48 patients died, 29 developed distant metastasis, and 33 developed local recurrence. Higher histological grade was associated with greater systemic inflammation. After clinicopathological adjustment, mGPS 1–2 versus 0 (HR 1.99, 95% CI 1.03–3.83), CAR per 0.1-unit increase (HR 1.099, 95% CI 1.003–1.203), and NLR per 1-unit increase (HR 1.74, 95% CI 1.17–2.60) were associated with poorer OS. For distant metastasis, all three markers showed adverse point estimates, although their 95% CIs included unity; no clear adjusted association was observed with local recurrence. Adding inflammatory markers increased the apparent Harrell C-index by only 0.009–0.014.

Conclusions

Preoperative mGPS, CAR, and NLR were associated with OS after clinicopathological adjustment but provided only limited incremental prognostic information. Their associations differed across clinical endpoints, supporting their use as adjuncts to, rather than replacements for, established histological, anatomical, and surgical prognostic factors.

Novelty statement:

This study extends previous chondrosarcoma evidence by evaluating systemic inflammatory markers specifically in surgically treated pelvic chondrosarcoma, separating metastatic and local failure using

competing-risk methods, and quantifying their incremental prognostic value beyond established clinicopathological factors.

Background

Chondrosarcoma is the second most common primary malignant bone tumour and remains principally a surgical disease, as conventional chondrosarcoma is relatively resistant to cytotoxic chemotherapy and radiotherapy [1]. Pelvic chondrosarcoma presents particular challenges because tumours are often large at diagnosis, arise within anatomically constrained compartments, and require complex resections in which oncological clearance must be balanced against morbidity and function [2, 8]. Histological grade, tumour size, surgical margin, age, and dedifferentiated histology are among the principal determinants of outcome and remain central to clinical risk stratification [2–8].

These clinicopathological factors characterise tumour burden and local disease control but may not fully capture the systemic host response to malignancy. Routine blood tests provide readily available measures of systemic inflammation. C-reactive protein (CRP) reflects the acute-phase response, serum albumin is influenced by inflammation as well as nutritional and physiological status, and circulating neutrophil and lymphocyte counts provide a pragmatic measure of innate–adaptive immune balance. The modified Glasgow Prognostic Score (mGPS) combines CRP and albumin within a standardised scoring system [9, 10], the CRP-to-albumin ratio (CAR) expresses the same components continuously, and the neutrophil-to-lymphocyte ratio (NLR) provides a complementary leukocyte-based measure of systemic inflammation [11]. Elevated CRP and NLR have been associated with adverse outcomes in bone and soft-tissue sarcoma [11, 12], and chondrosarcoma-specific studies have also reported prognostic associations for CRP and NLR [13–16].

More recently, Ben Gal et al. evaluated 549 patients across seven UK bone sarcoma units and showed that preoperative mGPS stratified overall survival across histological grades [17]. This multicentre study provides important chondrosarcoma-specific external support for mGPS, but it was not restricted to pelvic primary tumours and focused principally on survival. Two clinically relevant questions therefore remain. First, it is uncertain whether systemic inflammatory markers show similar associations with distant metastatic failure and local recurrence, outcomes that are governed by partly different biological and surgical determinants. Second, it remains unclear whether these markers provide meaningful prognostic information beyond established clinicopathological factors. This distinction is important because an association that persists after multivariable adjustment does not necessarily translate into improved patient-level discrimination or clinical utility.

We therefore evaluated preoperative systemic inflammation in a specialist-centre cohort of patients undergoing surgery for primary pelvic chondrosarcoma. mGPS was designated the principal inflammatory marker because it is standardised, integrates CRP and albumin, and has the strongest chondrosarcoma-specific external support; CAR and NLR were assessed in parallel as complementary measures. We examined the relationships of these markers with histological grade and overall survival

(OS), evaluated their associations with distant metastasis and local recurrence separately, and quantified their incremental prognostic contribution beyond a fixed clinicopathological model incorporating age, tumour size, histological grade, surgical margin, and dedifferentiated histology.

Methods

Study design and setting

This single-centre retrospective cohort study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [18]. The study used de-identified routine-care records from a tertiary orthopaedic oncology referral centre. The institutional ethics committee approved the study, waived individual informed consent, and the study complied with the Declaration of Helsinki.

Participants

The analytic cohort comprised 110 patients who underwent definitive surgery for primary pelvic chondrosarcoma between January 2014 and December 2021. Eligibility required a primary tumour arising from the pelvic bones, histological confirmation from the resection specimen, surgery at the study centre, a complete routine blood count and biochemical panel obtained within 14 days before surgery, and follow-up sufficient to determine event or censoring dates. The cohort included conventional, dedifferentiated, mesenchymal, clear-cell, and periosteal chondrosarcoma.

Patients with documented acute infection or fever within 14 days before surgery, preoperative antibiotic treatment for infection, haematological disease, another active malignancy, preoperative transfusion, or major recent surgery or trauma were not included. Chronic inflammatory or organ disease and preoperative antitumour treatment were recorded and addressed in sensitivity analyses rather than used as blanket exclusion criteria.

Pathology and operative variables

Diagnosis, histological subtype, and grade were abstracted from final resection pathology reports issued by specialist musculoskeletal pathologists and harmonised to contemporary bone-tumour nomenclature [19]. Histological grade was classified as grade 1, 2, or 3. Dedifferentiated histology was additionally coded as a separate variable because of its distinct biological behaviour. Surgical margins were classified as R0, R1, or R2; R1 and R2 were combined for regression analyses because of the small R2 group. Maximum tumour diameter was recorded in centimetres from the resection pathology report or, when unavailable, from preoperative cross-sectional imaging.

Inflammatory and nutritional markers

The blood sample obtained closest to surgery within the 14-day preoperative window was used. CRP was measured in mg/L and albumin in g/L; absolute neutrophil and lymphocyte counts were obtained from the same routine blood count. CAR was calculated as CRP divided by albumin, and NLR as the absolute neutrophil count divided by the absolute lymphocyte count. mGPS was assigned as 0 when CRP was ≤ 10 mg/L, 1 when CRP was > 10 mg/L and albumin was ≥ 35 g/L, and 2 when CRP was > 10 mg/L and albumin was < 35 g/L [9, 10].

mGPS was the principal inflammatory marker, with CAR and NLR evaluated in parallel as complementary measures. For regression analyses, mGPS was evaluated as 1–2 versus 0, CAR continuously per 0.1-unit increase, and NLR continuously per 1-unit increase. No data-driven cut-points were used in adjusted analyses. Cohort medians were used only for descriptive Kaplan–Meier visualisation of CAR and NLR. The prognostic nutritional index (PNI) and systemic immune-inflammation index (SII) were calculated for exploratory correlation analyses only and were not evaluated as candidate prognostic markers.

Outcomes and follow-up

Overall survival (OS) was the primary outcome and was measured from the date of surgery to death from any cause; patients alive at last contact were censored on that date. Distant metastasis was defined as the first radiologically or pathologically confirmed distant metastatic event, and local recurrence as the first recurrence within the operative bed or contiguous local compartment. Administrative follow-up ended on 15 March 2026. Median follow-up was estimated using the reverse Kaplan–Meier method.

For distant metastasis and local recurrence, absolute event probabilities were estimated using Aalen–Johansen cumulative incidence functions, with death before the event treated as a competing event [22]. Cause-specific Cox proportional-hazards models were used for regression analyses, with patients who died before the event censored at death. Cumulative-incidence and cause-specific hazard analyses were interpreted as complementary measures of absolute event probability and cause-specific association, respectively.

Statistical analysis

Continuous variables are reported as median (IQR) and categorical variables as number (percentage). Associations between mGPS category and histological grade were assessed using the Fisher–Freeman–Halton exact test, and CRP, albumin, CAR, and NLR were compared across grades using the Kruskal–Wallis test. Pairwise associations among clinicopathological and inflammatory variables were summarised using Spearman rank correlation coefficients. Unadjusted OS was estimated using the Kaplan–Meier method and compared using log-rank tests [20].

A clinicopathological reference Cox model included age (continuous), maximum tumour diameter (continuous), histological grade (grades 2 and 3 versus grade 1), surgical margin (R1/R2 versus R0), and dedifferentiated histology (versus other histologies) [21]. Each inflammatory marker was added

separately to this model to generate three extended models. The markers were not entered simultaneously because mGPS and CAR share CRP and albumin components, resulting in substantial conceptual and statistical overlap. Tied event times were handled using the Breslow approximation. Hazard ratios (HRs), 95% confidence intervals (CIs), and P values are reported.

Proportional-hazards assumptions were assessed using Schoenfeld residual diagnostics, and collinearity was evaluated using variance inflation factors. The linear functional form of CAR and NLR was assessed by likelihood-ratio comparison with models additionally containing a quadratic term. Grade-stratified analyses incorporated marker-by-grade interaction terms. Histology-based sensitivity analyses evaluated conventional chondrosarcoma alone and the cohort after exclusion of dedifferentiated histology using adjusted models. Given the small dedifferentiated subgroup, analyses restricted to dedifferentiated chondrosarcoma were univariable. Additional sensitivity analyses excluded patients with chronic inflammatory/autoimmune or chronic hepatic/renal disease and, separately, those who had received preoperative antitumour treatment.

Incremental prognostic performance was assessed by adding each inflammatory marker separately to the clinicopathological reference model. Because model performance was evaluated in the same cohort in which the models were fitted, discrimination and calibration are reported as apparent performance. Harrell C-indices and percentile 95% CIs were estimated from 2,000 patient-level bootstrap resamples, with paired changes in C-index calculated from the same resamples [23, 24]. Relative model fit was assessed using the Akaike information criterion (AIC) [25]. Apparent 5-year calibration was examined by grouping predicted mortality risk into quintiles and comparing predicted risk with Kaplan–Meier estimates of observed 5-year mortality. Exploratory 5-year decision-curve analysis used inverse-probability-of-censoring weighting [26, 27].

Key analysis variables were complete, and no imputation was performed. Given the limited numbers of distant metastases and local recurrences, secondary-outcome and subgroup analyses were considered exploratory. All tests were two-sided, and effect estimates are presented with 95% CIs and exact P values. No formal adjustment for multiplicity was applied; secondary, subgroup, and sensitivity analyses were interpreted accordingly. Analyses were performed using Python 3.13.5 with statsmodels 0.14.6, SciPy 1.17.0, and NumPy 2.3.5.

Results

Cohort characteristics and outcomes

The analytic cohort comprised 110 patients. Median age was 51.5 years (IQR 43.0–60.8), 70 patients (63.6%) were male, and median maximum tumour diameter was 9.7 cm (IQR 8.5–12.0). Histological grade was grade 1 in 22 patients (20.0%), grade 2 in 62 (56.4%), and grade 3 in 26 (23.6%). Conventional chondrosarcoma accounted for 89 cases (80.9%) and dedifferentiated chondrosarcoma for 12 (10.9%);

the remaining nine comprised mesenchymal, clear-cell, and periosteal subtypes. R0 resection was achieved in 88 patients (80.0%), with R1 and R2 margins in 19 and three patients, respectively (Table 1).

Table 1
Cohort characteristics and outcomes (n = 110)

Characteristic	Value
Age, years	51.5 (43.0–60.8)
Male sex	70 (63.6%)
Maximum tumour diameter, cm	9.7 (8.5–12.0)
Histological grade	
Grade 1	22 (20.0%)
Grade 2	62 (56.4%)
Grade 3	26 (23.6%)
Histological subtype	
Conventional	89 (80.9%)
Dedifferentiated	12 (10.9%)
Mesenchymal	4 (3.6%)
Clear-cell	3 (2.7%)
Periosteal	2 (1.8%)
Surgical margin	
R0	88 (80.0%)
R1	19 (17.3%)
R2	3 (2.7%)
mGPS category	
0	72 (65.5%)
1	25 (22.7%)
2	13 (11.8%)
CRP, mg/L	7.98 (5.04–13.09)
Albumin, g/L	40.16 (37.97–42.16)
CAR	0.198 (0.125–0.375)
NLR	2.39 (1.91–3.03)
Values are median (IQR) or number (%), unless otherwise stated. CAR, C-reactive protein-to-albumin ratio; CI, confidence interval; CRP, C-reactive protein; mGPS, modified Glasgow Prognostic Score; NLR, neutrophil-to-lymphocyte ratio.	

Characteristic	Value
Preoperative blood-to-surgery interval, days	7 (4–11)
Median follow-up, months	87.5
Deaths	48 (43.6%)
Distant metastases	29 (26.4%)
Local recurrences	33 (30.0%)
5-year overall survival	59.8% (95% CI 50.0%–68.3%)
Values are median (IQR) or number (%), unless otherwise stated. CAR, C-reactive protein-to-albumin ratio; CI, confidence interval; CRP, C-reactive protein; mGPS, modified Glasgow Prognostic Score; NLR, neutrophil-to-lymphocyte ratio.	

Median follow-up estimated by the reverse Kaplan–Meier method was 87.5 months. During follow-up, 48 patients died, 29 developed distant metastasis, and 33 developed local recurrence. Estimated 5-year OS was 59.8% (95% CI 50.0%–68.3%). The 5-year cumulative incidences of distant metastasis and local recurrence, with death treated as a competing event, were 24.6% and 29.4%, respectively.

Systemic inflammatory markers according to histological grade

Systemic inflammatory markers differed across histological grades (Fig. 1; Supplementary Table S1). The distribution of mGPS varied by grade (exact $P = 0.012$). mGPS 0 was present in 19 of 22 grade-1 tumours (86.4%), 42 of 62 grade-2 tumours (67.7%), and 11 of 26 grade-3 tumours (42.3%), whereas mGPS 2 was absent in grade 1 and present in six grade-2 (9.7%) and seven grade-3 tumours (26.9%).

Median CAR increased from 0.101 (IQR 0.075–0.153) in grade 1 to 0.191 (0.145–0.311) in grade 2 and 0.304 (0.216–0.751) in grade 3 ($P < 0.001$). Median NLR was 2.15 (1.78–2.57), 2.31 (1.82–2.78), and 3.12 (2.67–3.39) in grades 1, 2, and 3, respectively ($P < 0.001$). CRP increased and albumin decreased across grades (both $P < 0.001$).

Marker correlations are shown in Supplementary Figure S1. CAR was very strongly correlated with CRP (Spearman $\rho = 0.995$), while mGPS correlated strongly with CRP ($\rho = 0.825$) and CAR ($\rho = 0.823$). NLR showed moderate correlations with CAR ($\rho = 0.397$) and mGPS ($\rho = 0.372$) and a strong correlation with SII ($\rho = 0.891$).

Unadjusted overall survival

Unadjusted OS differed across mGPS categories (log-rank $P < 0.001$) (Fig. 2A). Kaplan–Meier curves also differed between the descriptive median-based groups for CAR ($P < 0.001$) and NLR ($P = 0.003$) (Fig. 2B,C). Median-based groups were used for visualisation only; adjusted analyses used the mGPS 1–2 versus 0 comparison and continuous CAR and NLR terms.

Adjusted associations with overall survival

After adjustment for age, tumour diameter, histological grade, surgical margin, and dedifferentiated histology, each inflammatory marker was associated with OS when added separately to the clinicopathological reference model (Table 2; Fig. 3A). mGPS 1–2 versus 0 was associated with a higher hazard of death (HR 1.99, 95% CI 1.03–3.83; P = 0.040). The HR was 1.099 per 0.1-unit increase in CAR (95% CI 1.003–1.203; P = 0.042) and 1.74 per 1-unit increase in NLR (95% CI 1.17–2.60; P = 0.007). Continuous-effect displays for CAR and NLR are shown in Fig. 3B and Fig. 3C.

Table 2
Adjusted associations with overall survival

Variable	HR (95% CI)	P value	Source model
Age, per year	1.04 (1.01–1.07)	0.008	Clinical baseline
Maximum tumour diameter, per cm	1.11 (0.99–1.25)	0.074	Clinical baseline
Grade 2 vs grade 1	2.80 (0.82–9.59)	0.101	Clinical baseline
Grade 3 vs grade 1	4.24 (1.12–15.97)	0.033	Clinical baseline
R1/R2 vs R0	1.05 (0.50–2.22)	0.898	Clinical baseline
Dedifferentiated vs other histology	4.00 (1.78–8.97)	< 0.001	Clinical baseline
mGPS 1–2 vs 0	1.99 (1.03–3.83)	0.040	Baseline + mGPS
CAR, per 0.1-unit increase	1.099 (1.003–1.203)	0.042	Baseline + CAR
NLR, per 1-unit increase	1.74 (1.17–2.60)	0.007	Baseline + NLR
The clinical baseline model contained age, maximum tumour diameter, histological grade, surgical margin, and dedifferentiated histology. Each inflammatory marker was added separately; mGPS, CAR, and NLR were not entered simultaneously. Ties were handled with the Breslow approximation. HR, hazard ratio; CI, confidence interval.			

In the clinicopathological reference model, older age was associated with poorer OS (HR 1.04 per year, 95% CI 1.01–1.07), as were grade 3 disease versus grade 1 (HR 4.24, 95% CI 1.12–15.97) and dedifferentiated histology versus other histologies (HR 4.00, 95% CI 1.78–8.97). The HRs were 1.11 per cm increase in tumour diameter (95% CI 0.99–1.25) and 1.05 for R1/R2 versus R0 margin status (95% CI 0.50–2.22) (Table 2). Model diagnostic findings, including collinearity and functional-form assessments, are summarised in Supplementary Table S3.

Distant metastasis and local recurrence

Competing-risk cumulative incidence curves are shown in Supplementary Figure S2. At 5 years, the cumulative incidence of distant metastasis was 19.6% for mGPS 0 and 34.2% for mGPS 1–2. Corresponding estimates were 18.4% versus 30.9% for the descriptive low- versus high-CAR groups and 18.4% versus 30.9% for the low- versus high-NLR groups. For local recurrence, the corresponding 5-year

cumulative incidences were 28.0% versus 32.6% for mGPS, 27.3% versus 32.3% for CAR, and 32.9% versus 25.7% for NLR. Median-based CAR and NLR groups were used for descriptive visualisation only.

In cause-specific Cox models, all three inflammatory-marker HRs for distant metastasis were above 1.0, although their 95% CIs included 1.0 (Table 3; Fig. 4A). The HR was 2.07 for mGPS 1–2 versus 0 (95% CI 0.89–4.82; $P = 0.091$), 1.11 per 0.1-unit increase in CAR (95% CI 0.99–1.24; $P = 0.083$), and 1.63 per 1-unit increase in NLR (95% CI 0.98–2.70; $P = 0.058$). In the clinicopathological reference model, tumour diameter was associated with the cause-specific hazard of distant metastasis (HR 1.24 per cm, 95% CI 1.06–1.45), as was grade 3 disease versus grade 1 (HR 7.51, 95% CI 1.47–38.35).

Table 3
Cause-specific associations with distant metastasis and local recurrence

Variable	Distant metastasis HR (95% CI)	P value	Local recurrence HR (95% CI)	P value
Clinicopathological baseline				
Age, per year	0.99 (0.96–1.03)	0.645	1.03 (0.99–1.06)	0.118
Maximum tumour diameter, per cm	1.24 (1.06–1.45)	0.008	1.15 (0.99–1.34)	0.070
Grade 2 vs grade 1	2.93 (0.65–13.17)	0.161	1.80 (0.66–4.90)	0.247
Grade 3 vs grade 1	7.51 (1.47–38.35)	0.015	2.02 (0.55–7.40)	0.288
R1/R2 vs R0	1.01 (0.37–2.75)	0.991	9.86 (4.39–22.14)	< 0.001
Dedifferentiated vs other histology	1.31 (0.39–4.44)	0.661	0.26 (0.05–1.31)	0.103
Inflammatory marker (separate extended models)				
mGPS 1–2 vs 0	2.07 (0.89–4.82)	0.091	1.66 (0.76–3.61)	0.200
CAR, per 0.1-unit increase	1.11 (0.99–1.24)	0.083	1.10 (0.96–1.27)	0.185
NLR, per 1-unit increase	1.63 (0.98–2.70)	0.058	0.78 (0.45–1.36)	0.384
Clinical rows are from outcome-specific baseline models. Marker rows are from three separate extended models adjusted for the same clinicopathological variables. Death before the event was censored at death, so estimates are cause-specific HRs. Absolute risks were separately estimated using Aalen–Johansen cumulative incidence with death as a competing event. The distant-metastasis and local-recurrence models contained 29 and 33 events, respectively, and are exploratory.				

For local recurrence, the HR was 1.66 for mGPS 1–2 versus 0 (95% CI 0.76–3.61; $P = 0.200$), 1.10 per 0.1-unit increase in CAR (95% CI 0.96–1.27; $P = 0.185$), and 0.78 per 1-unit increase in NLR (95% CI 0.45–

1.36; $P = 0.384$) (Table 3; Fig. 4B). R1/R2 margin status was associated with a higher cause-specific hazard of local recurrence compared with R0 resection (HR 9.86, 95% CI 4.39–22.14; $P < 0.001$).

Subgroup and sensitivity analyses

Grade-stratified analyses showed no evidence of marker-by-grade interaction for mGPS (P for interaction = 0.700), CAR ($P = 0.158$), or NLR ($P = 0.255$) (Fig. 5A; Supplementary Table S2). Only three deaths occurred among the 22 patients with grade-1 disease, resulting in wide confidence intervals for estimates in this subgroup.

Histology-based sensitivity analyses are shown in Fig. 5B and Supplementary Table S2. Among patients with conventional chondrosarcoma, HRs for OS were 1.80 (95% CI 0.88–3.68) for mGPS, 1.23 (95% CI 1.06–1.43) for CAR, and 1.88 (95% CI 1.18–3.00) for NLR. After exclusion of dedifferentiated chondrosarcoma, the corresponding HRs were 1.96 (95% CI 1.00–3.87), 1.19 (95% CI 1.06–1.33), and 1.90 (95% CI 1.24–2.92), respectively. Analyses restricted to the 12 patients with dedifferentiated chondrosarcoma were univariable.

Exclusion of patients with chronic inflammatory/autoimmune or chronic hepatic/renal disease yielded estimates similar to those of the primary OS analyses. Results were also similar after exclusion of the two patients who had received preoperative antitumour treatment (Supplementary Table S4).

Incremental prognostic performance

The clinicopathological reference model had an apparent Harrell C-index of 0.775 (95% CI 0.705–0.844) (Table 4; Fig. 6A). The apparent C-index was 0.785 (95% CI 0.716–0.852) after addition of mGPS, 0.785 (95% CI 0.717–0.853) after addition of CAR, and 0.790 (95% CI 0.717–0.860) after addition of NLR. Corresponding changes from the reference model were + 0.009, + 0.010, and + 0.014, respectively; paired bootstrap 95% CIs for all three changes included zero (Fig. 6B).

Table 4
Apparent model performance and incremental prognostic information for overall survival

Model	Harrell C-index (95% CI)	Δ C-index vs baseline	AIC	Δ AIC vs baseline
Clinical baseline	0.775 (0.705–0.844)	Reference	385.2	Reference
Clinical baseline + mGPS	0.785 (0.716–0.852)	+ 0.009	383.2	–2.1
Clinical baseline + CAR	0.785 (0.717–0.853)	+ 0.010	383.5	–1.8
Clinical baseline + NLR	0.790 (0.717–0.860)	+ 0.014	380.2	–5.0
All performance estimates are apparent because models were developed and evaluated in the same cohort. C-index 95% CIs were obtained by patient-level bootstrap. Paired bootstrap intervals for all Δ C-index estimates included zero. Lower AIC indicates better relative fit. AIC, Akaike information criterion; CI, confidence interval.				

AIC decreased from 385.2 for the clinicopathological reference model to 383.2 after addition of mGPS, 383.5 after addition of CAR, and 380.2 after addition of NLR, corresponding to Δ AIC values of – 2.1, – 1.8, and – 5.0, respectively (Fig. 6B).

Predicted and observed 5-year mortality were broadly aligned across predicted-risk quintiles in the apparent calibration analysis (Fig. 6C). Exploratory IPCW decision curves for the clinicopathological reference and marker-extended models largely overlapped across the evaluated threshold probabilities (Fig. 6D).

Discussion

This study defines a focused role for preoperative systemic inflammation in pelvic chondrosarcoma. Systemic inflammatory burden increased with histological grade, and mGPS, CAR, and NLR each remained associated with OS after clinicopathological adjustment. For distant metastasis, all three markers yielded adverse point estimates, although these associations were less precise than those for OS, whereas no clear adjusted association was observed with local recurrence. Importantly, adding inflammatory markers to the clinicopathological reference model produced only small gains in apparent discrimination. Taken together, these findings suggest that systemic inflammation reflects an additional dimension of aggressive tumour–host biology, but contributes only modest incremental prognostic information once established clinicopathological factors are considered.

These findings should be interpreted in the context of recent multicentre evidence. Ben Gal et al. evaluated 549 patients from seven collaborating UK bone sarcoma units and showed that preoperative mGPS stratified overall survival across histological grades [17]. The present study addresses a complementary question rather than simply reproducing that analysis in a smaller cohort. It focuses

specifically on surgically treated pelvic primary tumours, evaluates mGPS alongside CAR and NLR, separates distant metastatic failure from local recurrence using competing-risk and cause-specific analyses, and directly quantifies the incremental prognostic contribution of inflammatory markers beyond a fixed clinicopathological reference model. This distinction is clinically relevant because persistence of an association after multivariable adjustment does not necessarily imply a meaningful improvement in patient-level prediction.

Among the three markers, mGPS remains the most defensible candidate for further validation because it is standardised, incorporates CRP and albumin, and now has chondrosarcoma-specific multicentre support [9, 10, 17]. The present data, however, do not demonstrate superiority of mGPS over CAR or NLR. Indeed, NLR showed the strongest nominal association with OS and the largest apparent reduction in AIC in this cohort. CAR also remained associated with OS, but its near-perfect correlation with CRP ($\rho = 0.995$) indicates substantial overlap with CRP variation. Accordingly, the present analysis does not establish incremental prognostic value of CAR beyond CRP itself.

The association between systemic inflammation and histological grade is biologically plausible, although its underlying mechanism cannot be determined from these data. mGPS reflects the combination of CRP and albumin within an established systemic inflammation-based score [9, 10], whereas NLR represents a complementary leukocyte-based inflammatory measure. Previous studies have linked elevated CRP to adverse outcomes in primary bone sarcoma and chondrosarcoma [12–14], while higher NLR has been associated with poorer survival in both dedifferentiated and conventional chondrosarcoma [15, 16]. The greater inflammatory burden observed in higher-grade tumours in the present cohort may therefore accompany more aggressive tumour biology, but should not be interpreted as evidence that systemic inflammation itself causes progression. These markers may also incorporate effects of tumour burden, comorbidity, physiological status, medication exposure, and other unmeasured host factors.

The differing patterns for distant metastasis and local recurrence are also informative. All three inflammatory markers showed adverse point estimates for distant metastasis, while tumour size and histological grade were important clinicopathological correlates of metastatic failure. By contrast, local recurrence was much more closely associated with surgical margin status in this cohort: R1/R2 margins were associated with an approximately ten-fold higher cause-specific hazard of local recurrence, whereas the estimates for mGPS, CAR, and NLR were imprecise and inconsistent. This endpoint-specific pattern is compatible with previous evidence demonstrating the importance of surgical margins in chondrosarcoma [7] and, more specifically, in pelvic chondrosarcoma [8]. These findings support a conceptual distinction between systemic biological risk and local surgical control rather than a single inflammatory process governing both outcomes.

The incremental prediction analyses provide an important constraint on clinical interpretation. Although mGPS, CAR, and NLR each remained associated with OS after clinicopathological adjustment, adding these markers increased the apparent C-index by only 0.009–0.014, and the paired bootstrap intervals

for all three changes included zero. Apparent calibration was assessed only within the same cohort in which the models were fitted, and the exploratory decision curves largely overlapped. Statistical prognostic association should therefore not be equated with clinically meaningful incremental prediction. At present, systemic inflammatory markers may complement conventional risk assessment, but the present data do not support their use in isolation to guide operative strategy or surveillance decisions.

Several features strengthen this study. The cohort was restricted to surgically treated pelvic chondrosarcoma at a specialist orthopaedic oncology centre, and the inflammatory measurements were derived from routinely available preoperative blood tests. The clinicopathological reference model was fixed without data-driven variable selection, regression analyses avoided data-derived cut-points, and overlap among inflammatory markers was explicitly considered. Distant metastasis and local recurrence were evaluated using methods that accounted for death as a competing event when estimating absolute event probabilities, and prognostic association was explicitly distinguished from incremental predictive performance. The endpoint-specific findings were also clinically coherent, with age, grade, and dedifferentiated histology associated with OS, tumour size and grade associated with distant metastasis, and surgical margin strongly associated with local recurrence.

Several limitations should temper interpretation. The retrospective single-centre design is susceptible to selection bias, measurement error, and residual confounding. Histological subtype and grade were obtained from routine specialist pathology reports without a study-specific blinded central review. Inflammatory markers were measured at a single preoperative time point and may vary over time. Although patients with documented acute infection and major haematological confounders were excluded, chronic inflammatory conditions and other unmeasured exposures cannot be fully accounted for. The sample size also limited model precision: the OS models contained approximately 6.9 deaths per regression parameter, whereas the cause-specific models for distant metastasis and local recurrence contained fewer than five events per parameter. Secondary-outcome, subgroup, and restricted-histology analyses should therefore be regarded as exploratory. In addition, multiple analyses were performed without formal multiplicity adjustment, and discrimination, calibration, and decision-curve analyses were evaluated in the same cohort in which the models were fitted. Bootstrap intervals quantify sampling uncertainty but do not provide external validation or complete correction for model optimism.

The appropriate next step is multicentre external validation rather than further optimisation within this cohort. Future studies should harmonise laboratory timing, pathology assessment, and definitions of local and metastatic events; retain competing-risk methods for absolute-risk estimation; and evaluate discrimination, calibration, and clinical net benefit against clearly defined clinicopathological reference models. Repeated perioperative measurements may also determine whether inflammatory trajectories provide information beyond a single preoperative value. Until such validation is available, mGPS is best regarded as a readily available adjunctive prognostic marker with the strongest current chondrosarcoma-

specific external support, while CAR and NLR provide complementary measures that require further validation.

Conclusions

Higher histological grade in pelvic chondrosarcoma was associated with greater systemic inflammation. Preoperative mGPS, CAR, and NLR were each associated with OS after clinicopathological adjustment, with mGPS remaining the candidate with the strongest current chondrosarcoma-specific external support. Associations with distant metastasis were directionally adverse but less precise than those for OS, whereas no inflammatory marker showed a clear adjusted association with local recurrence. Established clinicopathological factors remained central to prognostic assessment, with their associations differing across clinical endpoints. Importantly, the inflammatory markers provided only small increments in apparent predictive performance. These markers should therefore be considered adjuncts to, rather than replacements for, established histological, anatomical, and surgical prognostic factors.

Abbreviations

AIC

Akaike information criterion

CAR

C-reactive protein-to-albumin ratio

CI

confidence interval

CRP

C-reactive protein

HR

hazard ratio

IPCW

inverse-probability-of-censoring weighting

IQR

interquartile range

mGPS

modified Glasgow Prognostic Score

NLR

neutrophil-to-lymphocyte ratio

OS

overall survival

PNI

prognostic nutritional index

SII

systemic immune-inflammation index

STROBE

Strengthening the Reporting of Observational Studies in Epidemiology.

Declarations

Ethics approval

This study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of West China Hospital, Sichuan University. The requirement for individual informed consent to participate was waived by the Ethics Committee because of the retrospective design and use of de-identified clinical data.

Consent for publication

Not applicable.

Data and materials availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of interest

None.

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Authors' contributions

Mingzhong Xiao and Xiang Fang contributed equally to the conceptualization and design of the study, data acquisition and curation, statistical analysis, interpretation of the results, preparation of the figures and tables, and drafting of the manuscript. Hui Dong contributed to data acquisition, data verification, and interpretation of the results. Yan Xiong contributed to study methodology, clinical data collection, data interpretation, and critical revision of the manuscript. Senlin Lei contributed to follow-up data collection, data validation, and critical revision of the manuscript. Fuguo Kuang contributed to patient identification, clinical data acquisition, data validation, and critical review of the manuscript. Wenli Zhang contributed to study design, methodological guidance, supervision, project administration, interpretation of the findings, and critical revision of the manuscript. Hong Duan conceived and supervised the study, provided clinical and research resources, administered the project, interpreted the findings, and critically

revised the manuscript. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

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