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Original Research

Utility of Blood Cell Ratio Combinations for Diagnosis of Periprosthetic Joint Infection

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ABSTRACT

Background: Periprosthetic joint infection (PJI) is a serious complication following joint replacement surgery, and its diagnosis can be challenging due to the similarity of symptoms to other conditions and the lack of confirmatory imaging tests. Platelet/mean platelet volume ratio (PVR), platelet/lymphocyte ratio, monocyte/lymphocyte ratio, and neutrophil/lymphocyte ratio have been proposed as potential markers to aid in the diagnosis of PJI. This study aimed to further assess the utility of these blood cell ratio combinations for the diagnosis of PJI.

Methods: A retrospective chart review was conducted on patients who presented to a university hospital for evaluation for PJI or underwent aseptic revision surgery. All patients were reviewed for inclusion in the study. Data were collected on several markers, including complete blood counts, synovial fluid white blood cell count, and polymorphonuclear percentage. Receiver operator characteristic curve analysis was used to evaluate the diagnostic capabilities of the markers and marker combinations.

Results: The combination of erythrocyte sedimentation rate, C-reactive protein, synovial white blood cell count, and synovial polymorphonuclear percentage, with PVR, had the highest area under the curve of 0.97, with a sensitivity of 94.3% and a specificity of 88.9%, and a positive predictive value of 97.1% and a negative predictive value of 80.0%.

Conclusions: This study further supports the use of PVR calculated from complete blood count commonly ordered laboratory values obtained during routine complete blood counts when combined with established serum and synovial markers to increase the diagnostic accuracy for diagnosing PJI.

Introduction

Periprosthetic joint infection (PJI) is a serious complication following joint replacement surgery, such as total hip arthroplasty (THA) or total knee arthroplasty (TKA), with reported rates ranging from 1% to 2% [1]. The diagnosis of PJI can be challenging due to the similarity of symptoms to other conditions such as implant loosening and the lack of visibility on imaging tests [2]. Several markers have been proposed for the diagnosis of PJI, including laboratory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and synovial fluid analysis, including synovial white blood cell count (Syn. WBC) and polymorphonuclear neutrophils percentage (PMN%). However, the sensitivity (SN) and specificity (SP) of these markers alone are limited. [2]

Subsequent research has evaluated a number of different potential serum biomarkers for PJI diagnosis, including D-dimer [3,4], synovial alpha defensin [5–8], synovial leukocyte esterase [5,9,10], and synovial CRP [10,11]. The most promising synovial fluid biomarker for PJI appears to be alpha defensin [6,7], which was initially reported to have 100% SN and 96% SP in a comprehensive review and meta-analysis by Wyatt et al [5]. However, the wide adoption of the alpha defensin test is limited given its substantially high cost and availability, as testing is not available at most institutions [12,13]. In addition, more recent studies have found a considerably lower SN for alpha defensin than was previously reported, especially in low-virulence organisms [14,15]. Consequently, there is a need to utilize a commonly available, low-cost marker or marker combination.

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Blood cell ratios, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and platelet-to-volume ratio (PVR), which are easily calculated from routine complete blood count with differential, have been proposed as potential markers for infections [16–19]. The utility of these blood cell ratios for the diagnosis of PJI has not been fully established. Recently, studies have investigated the utility of combining blood cell ratios for the diagnosis of PJI. One study reported NLR had a diagnostic accuracy of 80% for PJI, with a SN of 85% and SP of 68% [20]. In contrast, Tirumala et al. found that the combination of ESR, CRP, Syn. WBC, and PMN% with PVR had a SN of 98.5% and a SP of 97.9% for knees, whereas with PLR, SN, and SP reached 99.03% and 98.8% for knees [21]. Similarly, Klemt et al. found that when either PVR or PLR were combined with the set of ESR, CRP, Syn. WBC, and PMN%, the accuracy, SN, and SP for PJI diagnosis in hips all reached above 97% [22].

These findings suggest that the combination of blood cell ratios may have improved diagnostic accuracy compared to the use of individual markers alone. However, it is not clear which combination of blood cell ratios is the most accurate for the diagnosis of PJI. The aim of this study was to investigate the utility of different combinations of blood cell ratios for the diagnosis of chronic PJI in an academic tertiary medical center with a diverse patient population.

Material and methods

Data collection

A retrospective chart review of patients who presented to a university hospital for evaluation for PJI or underwent an aseptic revision for TKA was included in this study. We identified patients with chronic PJI through a manual chart review of medical records, with the definition of PJI by the Infectious Diseases Society of America being used to classify chronic PJI (2019). We excluded patients with a diagnosis of acute PJI. We included patients who had a history of primary total joint arthroplasty, unicompartmental knee arthroplasty, septic and aseptic revisions, and two-stage reimplants septic revisions included debridement, antibiotics and implant retention, one-stage, and two-stage reimplantation. Aseptic revisions included revisions for instability, loosening, malalignment, and fracture. We excluded patients with a past medical history of rheumatoid arthritis, systemic lupus erythematosus, and metastatic cancer. Complete blood counts were used to collect neutrophil, lymphocyte, monocyte, and platelet counts and calculate the MLR, NLR, PLR, and PVR. We excluded patients with cell counts and inflammatory markers beyond 4 weeks before revision or workup for PJI. Syn. WBC and PMN% were also collected. The study received approval through the university's institutional review board.

Statistical analysis

All statistical analyses were performed using SAS (SAS Institute Inc., Cary, NC). The mean, standard deviation, and distribution for all serum and synovial markers were calculated. An independent t-test was used to compare the aseptic cohort (negative control) with the septic cohort. The receiver operating characteristic curves for all markers were analyzed to calculate the area under the curve (AUC), as well as the SN, SP, and positive and negative predictive values (PPV and NPV). The cutoff points for cell ratios (NLR, MLR, PVR, and PLR) were determined by Youden's index. We used the cutoff points for ESR, CRP, Syn. WBC, and PMN as determined by the Musculoskeletal Infection Society 2018 criteria for PJIs. The utility of combining cell ratios with serum markers and aspirate results was then assessed, again using the AUC, SN, SP, PPV, and NPV. McNemar's test was used to compare differences in SN and SP between markers and combinations. A *P*-value less than .05 was considered significant for all tests.

Results

A total of 577 patients were included in our study. There were a total of 247 patients (42.8%) with a diagnosis of PJI. The main difference in patient demographics between the 2 groups was the higher prevalence of PJIs among older patients, with 7.7% of the PJI group under 50 years of age, 80.6% between 50 and 79 years of age, and 11.7% between 80 and 99 years of age, compared to 10.3%, 77.6%, and 12% in the non-PJI group, respectively ($P = .54$). The gender and racial distributions were similar between the 2 groups, with roughly equal numbers of male and female patients in each group and a slightly higher proportion of white patients in the PJI group (81% vs 74.8% in the non-PJI group). The previous surgery was also similar, with THA and TKA being the most common in both groups and a small number of other procedures (irrigation and debridement, revision THA, revision TKA, replant TKA, unicompartmental knee replacement, manipulation under anesthesia) being performed in both groups (Table 1).

Mean and standard deviations for each serum and synovial marker are reported in Table 2. The aseptic group (n = 330) had lower levels of ESR (mean = 24.2 mm/h, standard deviation [SD] = 22.9), CRP (mean = 3.3 mg/L, SD = 8.4), Syn. WBC (mean = 2022.6 cells/μL, SD = 5825.4), synovial PMN% (mean = 37.84%, SD = 30.0), platelet count (mean = 244.5, SD = 87.3), mean platelet volume (MPV; mean = 8.6, SD = 1.0), lymphocyte count (mean = 1.7, SD = 0.7), monocyte count (mean = 0.7, SD = 0.5), neutrophil count (mean = 4.8, SD = 2.20), MLR (mean = 0.5, SD = 0.4), NLR (mean = 4.0, SD = 4.8), PVR (mean = 28.5, SD = 12.0), and PLR (mean =

Table 1
Patient demographics.

	Total		PJI			
			No		Yes	
	N	%	N	%	N	%
Total Patients	577	100	330	100	247	100
<50 y	53	9.2	34	10.3	19	7.7
50-79 y	455	78.9	256	77.6	199	80.6
80-99 y	69	12	40	12.1	29	11.7
Gender						
Female	293	50.8	168	50.9	125	50.6
Male	281	48.7	159	48.2	122	49.4
Unknown	3	0.5	3	0.9	.	.
Race						
White	447	77.5	247	74.8	200	81
Asian	5	0.9	4	1.2	1	0.4
Black	96	16.6	59	17.9	37	15
Other	24	4.2	15	4.5	9	3.6
Unknown	2	0.3	2	0.6	.	.
TJA						
THA	291	50.4	168	50.9	123	49.8
TKA	286	49.6	162	49.1	124	50.2
Index Surgery						
DAIR THA	12	2.1	2	0.6	10	4
DAIR TKA	6	1	1	0.3	5	2
RTHA	12	2.1	9	2.7	3	1.2
RTKA	11	1.9	7	2.1	4	1.6
Replant TKA	7	1.2	1	0.3	6	2.4
THA	265	45.9	156	47.3	109	44.1
TKA	260	45.1	151	45.8	109	44.1
UKA	3	0.5	3	0.9	.	.
MUA TKA	1	0.2	.	.	1	0.4

DAIR, debridement, antibiotics and implant retention; UKA, unicompartmental knee arthroplasty; MUA, manipulation under anesthesia.

Table 2
Serum and synovial markers for PJI and aseptic cohorts.

Preoperative marker	Aseptic group					PJI					*P*
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
ESR (mm/h)	24.15	22.85	16.00	1.50	129.00	70.02	33.52	70.50	2.00	140.00	**<.0001**
CRP (mg/L)	3.25	8.44	0.80	0.10	59.00	24.08	45.74	11.00	0.10	344.00	**<.0001**
Synovial WBC (cells/μL)	2022.59	5825.37	295.00	0.00	36,000.00	62,340.66	84,135.79	34,950.00	4.00	511,639.00	**<.0001**
PMN%	37.84	30.02	34.00	1.00	98.00	87.43	16.87	92.00	2.00	100.00	**<.0001**
Platelet count	244.45	87.26	241.50	3.30	727.00	305.87	136.46	289.00	38.00	929.00	**<.0001**
MVP	8.59	1.05	8.50	6.40	12.00	8.18	0.93	8.20	6.20	10.00	**.0003**
Lymphocyte count	1.68	0.70	1.60	0.30	4.10	1.35	0.75	1.25	0.10	5.40	**<.0001**
Monocyte count	0.66	0.52	0.60	0.10	6.40	0.81	0.37	0.70	0.20	2.30	**.0003**
Neutrophil count	4.84	2.20	4.20	0.40	13.00	7.43	4.05	6.60	0.00	24.00	**<.0001**
MLR	0.46	0.42	0.33	0.02	4.00	0.89	0.89	0.58	0.13	5.67	**<.0001**
NLR	3.97	4.76	2.65	0.31	40.00	10.29	19.06	5.00	0.00	205.00	**<.0001**
PVR	28.51	11.97	27.54	0.37	82.78	38.70	19.50	34.20	9.20	131.19	**<.0001**
PLR	177.46	116.96	152.94	1.50	826.00	310.04	292.18	217.93	53.59	2980.00	**<.0001**

MVP, mean platelet volume.
Bold values indicate statistical significance.

177.5, SD = 117.0) compared to the PJI group (n = 247). The PJI group had higher levels of ESR (mean = 70.0 mm/h, SD = 33.5), CRP (mean = 24.1 mg/L, SD = 45.7), Syn. WBC (mean = 62,340.7 cells/μL, SD = 84,135.8), synovial PMN% (mean = 87.4%, SD = 16.9), platelet count (mean = 305.9, SD = 136.5), MPV (mean = 8.2, SD = 0.9), lymphocyte count (mean = 1.4, SD = 0.8), monocyte count (mean = 0.8, SD = 0.4), neutrophil count (mean = 7.4, SD = 4.0), MLR (mean = 0.9, SD = 0.9), NLR (mean = 10.3, SD = 19.1), PVR (mean = 38.7, SD = 19.5), and PLR (mean = 310.0, SD = 292.2). The differences in all markers between the 2 groups were statistically significant ($P < .0001$).

The results of the receiver operating characteristic curve analysis for serum and synovial biomarkers in patients with PJIs are shown in Table 3. The AUC for NLR (AUC = 0.72, SN = 52.5%, SP = 82.2%, PPV = 71.3%, NPV = 67.2%), MLR (AUC = 0.72, SN = 66.5%, SP = 69.4%, PPV = 65.4%, NPV = 70.5%), PVR (AUC = 0.66, SN = 46.4%, SP = 80.3%, PPV = 62.1%, NPV = 68.2%), and PLR (AUC = 0.70, SN = 58.3%, SP = 76.0%, PPV = 68.0%, NPV = 67.5%) were all found to be useful for identifying PJI. The AUC for ESR (AUC = 0.80, SN = 86.0%, SP = 74.0%, PPV = 79.6%, NPV = 81.8%) and CRP (AUC = 0.73, SN = 52.5%, SP = 92.9%, PPV = 89.9%, NPV = 62.3%) were also found to be useful when using cutoffs of 30 mm/h and 10 mg/L, respectively. The AUC for Syn. WBC (AUC = 0.86, SN = 86.8%, SP = 85.9%, PPV = 93.6%, NPV = 73.3%) and percent PMNs (AUC = 0.86, SN = 86.6%, SP = 85.3%, PPV = 93.5%, NPV = 72.2%) were also found to be useful when using cutoffs of 3000 cells/μL and 80%, respectively.

The results of the receiver operating characteristic curve analysis for biomarker combinations for patients with PJIs are shown in Table 4. The AUC for the combination of ESR and CRP was 0.86, with a SN of 90.5% and a SP of 71.2%. The combination of ESR, CRP, and PVR had an AUC of 0.88, with a SN of 90.3% and a SP of 74.6%. This combination had a significantly higher AUC compared to the combination of ESR and CRP alone (0.86). The combination of Syn. WBC and percent PMN had an AUC of 0.91, with a SN of 87.8% and a SP of 85.0%. When ESR, CRP, Syn. WBC, and PMN were combined, the AUC increased to 0.94, with a SN of 90.5% and a SP of 89.6%. The combination of ESR, CRP, Syn. WBC, and PMN with PVR had an AUC of 0.97, with a SN of 94.3% and a SP of 88.9%, and a PPV of 97.1% and a NPV of 80.0% (Supplementary Figure 1). This combination had a higher AUC compared to the combination of ESR, CRP, Syn. WBC, and PMN alone (0.94). The inclusion of PVR significantly improved the SP of the ESR + CRP combination and significantly improved the SN of the ESR + CRP + Syn. WBC + PMN combination ($P < .05$), Table 5.

Discussion

Despite the abundance of novel techniques used for the diagnosis of PJI, a single gold standard has yet to be established. A number of assays, such as D-dimer, synovial alpha defensin, synovial leukocyte esterase, and synovial CRP, have been discussed in current literature [11,12,23], and while each method has its advantages, it also has its drawbacks as well. Current methods can produce ambiguous results, take days to weeks to complete, and be costly to run [24,25]. Recent studies have evaluated the use of readily available serum predictors of inflammation such as neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), and platelet/mean platelet volume ratio (PVR) in combination with established serum and synovial markers to improve the diagnostic accuracy for PJI. These ratios represent commonly ordered laboratory values obtained during a routine complete blood count with differential and are thus cost-effective.

Our findings support the use of PVR along with established serum and synovial markers to improve the diagnosis of PJI. The combination of ESR and CRP in our cohort was found to have an AUC of 0.86, a SN of 90.48, and a SP of 71.21%. The addition of PVR to this combination improved the AUC to 0.88 and SP to 74.55%, while

Table 3
ROC curves for serum and synovial biomarkers for patients with PJI.

	NLR	MLR	PVR	PLR	ESR (>30)	CRP (>10)	Syn. WVC (>3000)	PMN (>80)
AUC	0.72	0.72	0.6565	0.70	0.80	0.73	0.86	0.86
Cutoff point	4.77	0.45	36.79	200.57	30.00	10.00	3000.00	80.00
Sensitivity	52.47	66.52	46.38	58.26	86.02	52.54	86.84	86.58
Specificity	82.20	69.43	80.30	75.95	74.00	92.96	85.94	85.25
PPV	71.34	65.38	62.14	68.02	79.61	89.86	93.62	93.48
NPV	67.18	70.50	68.24	67.46	81.77	62.29	73.33	72.22

ROC, receiver operating characteristic.

Table 4
Sensitivity and specificity of biomarker combinations.

Blood cell ratio combinations	AUC	Sensitivity	Specificity	PPV	NPV
ESR + CRP	0.86	90.48	71.21	78.57	86.50
Syn. WBC + PMN	0.91	87.76	85.00	93.48	73.91
ESR + CRP + Syn. WBC + PMN	0.94	90.51	89.58	96.12	76.79
ESR + CRP + NLR	0.87	83.08	75.93	81.07	78.34
ESR + CRP + MLR	0.87	91.35	65.85	77.24	85.71
ESR + CRP + PVR	0.88	90.32	74.55	80.00	87.23
ESR + CRP + PLR	0.86	72.12	86.50	87.21	70.85
ESR + CRP + NLR + MLR	0.87	84.08	74.07	80.09	78.95
ESR + CRP + NLR + MLR + PVR	0.88	71.03	87.91	87.36	72.07
ESR + CRP + NLR + MLR + PVR + PLR	0.88	69.16	91.21	90.24	71.55
ESR + CRP + MLR + PVR	0.88	74.07	85.71	86.02	73.58
ESR + CRP + MLR + PVR + PLR	0.88	93.52	64.84	75.94	89.39
ESR + CRP + PVR + PLR	0.87	74.07	86.81	86.96	73.83
ESR + CRP + PVR + NLR	0.89	72.90	87.91	87.64	73.39
ESR + CRP + PVR + PLR	0.87	74.07	86.81	86.96	73.83
ESR + CRP + PLR + NLR	0.87	83.58	75.78	81.16	78.71
ESR + CRP + Syn. WBC + PMN + NLR	0.93	89.74	89.47	96.33	73.91
ESR + CRP + Syn. WBC + PMN + MLR	0.94	90.98	89.74	96.52	76.09
ESR + CRP + Syn. WBC + PMN + PVR	0.97	94.29	88.89	97.06	80.00
ESR + CRP + Syn. WBC + PMN + PLR	0.95	90.16	89.74	96.49	74.47

SN remained relatively the same at 90.32%. Furthermore, the combination of ESR, CRP, Syn. WBC, and PMN% was found to have an AUC of 0.94, a SN of 90.51%, and a SP of 89.58%. Similarly, the addition of PVR to this combination improved the diagnostic accuracy with an AUC of 0.97, a SN of 94.3%, and a SP of 88.9% for predicting PJI.

Tirumala et al. and Klemt et al. found that both PVR and PLR had a high AUC and increased SN and SP for predicting PJI in knees and hips, respectively [21,22]. In contrast, in our cohort, the combination of serum and synovial makers with PLR did not increase the diagnostic accuracy. However, our analysis includes knees, hips, and patients who have undergone revision or reimplantation in the past. Additionally, we expanded our blood test collection time to within 4 weeks prior to aspiration or revision surgery. Despite these differences, we also found that PVR was associated with the pathophysiological state of PJI and improved its diagnostic accuracy when combined with established serum and synovial markers. This is important given that there are multiple variables, such as time from blood collection to measurement and anticoagulant used, that can affect the variability of these results. With a different patient population, laboratory, and more broad inclusion criteria, this study serves as supporting evidence for the use of PVR to aid in the diagnosis of PJI.

Currently, synovial alpha defensin and leukocyte esterase have been proposed as novel markers with high diagnostic accuracy to

Table 5
Comparison of sensitivity and specificity between markers.

Biomarker		Sensitivity *P*-value	Specificity *P*-value
ESR	NLR	**.0002**	.4426
ESR	MLR	**<.0001**	.6254
ESR	PLR	**<.0001**	.098
ESR	PVR	**<.0001**	.3771
CRP	NLR	**.0001**	**<.0001**
CRP	MLR	**.0031**	**<.0001**
CRP	PLR	.5856	**.0004**
CRP	PVR	.1882	.0872
ESR + CRP	ESR + CRP + NLR	**<.0001**	**<.0001**
ESR + CRP	ESR + CRP + MLR	**<.0001**	**<.0001**
ESR + CRP	ESR + CRP + PLR	**<.0001**	**<.0001**
ESR + CRP	ESR + CRP + PVR	.4799	**.0313**
ESR + CRP	ESR + CRP + NLR + MLR	**<.0001**	**<.0001**
ESR + CRP	ESR + CRP + NLR + MLR + PVR	.324	**<.0001**
ESR + CRP	ESR + CRP + NLR + MLR + PVR + PLR	.243	**<.0001**
ESR + CRP	ESR + CRP + MLR + PVR	.5224	**<.0001**
ESR + CRP	ESR + CRP + MLR + PVR + PLR	.243	**<.0001**
ESR + CRP	ESR + CRP + PVR + PLR	.5224	**<.0001**
ESR + CRP	ESR + CRP + PVR + NLR	.6358	**<.0001**
ESR + CRP	ESR + CRP + PLR + NLR	**<.0001**	**<.0001**
ESR + CRP	ESR + CRP + Syn. WBC + PMN + NLR	**.0092**	**<.0001**
ESR + CRP	ESR + CRP + Syn. WBC + PMN + MLR	**.03**	**<.0001**
ESR + CRP	ESR + CRP + Syn. WBC + PMN + PVR	**.0294**	**<.0001**
ESR + CRP	ESR + CRP + Syn. WBC + PMN + PLR	.2717	**<.0001**
ESR + CRP + Syn. WBC + PMN	ESR + CRP + Syn. WBC + PMN + NLR	**<.0001**	**<.0001**
ESR + CRP + Syn. WBC + PMN	ESR + CRP + Syn. WBC + PMN + MLR	**<.0001**	**<.0001**
ESR + CRP + Syn. WBC + PMN	ESR + CRP + Syn. WBC + PMN + PVR	**.0215**	**<.0001**
ESR + CRP + Syn. WBC + PMN	ESR + CRP + Syn. WBC + PMN + PLR	**<.0001**	**<.0001**

McNemar's test was used to compare differences in sensitivity and specificity between markers and combinations. A *P*-value less than .05 was considered significant for all tests.

aid in the diagnosis of PJI [26–28]. In a systematic review and meta-analysis, Chen et al. found that synovial alpha defensin and leukocyte esterase had the highest SN and SP for predicting PJI, with a pooled SN of 87% and 87% and SP of 96% and 97%, respectively [12]. PVR in combination with established serum and synovial markers yields nearly similar SNs and SPs, as evidenced by Tirumala et al., Klemt et al., and our study, without the associated high cost, timing, and limited availability [21,22].

It is important to consider the limitations of this study when interpreting the results. This was a retrospective chart review and may be subject to bias or a negligible amount of missing data. Additionally, we acknowledge that the MPV measurement is a parameter that has not been fully standardized and may be affected by multiple variables such as the timing of blood collection and the type of anticoagulant used. Despite this limitation, previous studies have reported the utility of MPV as a diagnostic marker for inflammation and PJIs [21,22,29–31]. Further, it is possible that the specific combination of markers found to be most sensitive and specific in this particular retrospective study may be a product of statistical chance. These findings should be validated with a prospective study and/or on a unique dataset.

Conclusions

The results of this study suggest that certain combinations of blood cell ratios and serum markers may be useful in the diagnosis of PJI. The combination of ESR, CRP, Syn. WBC, PMN, and PVR had the highest AUC for predicting PJI (AUC 0.97), with a SN of 94.3% and SP of 88.9%. The addition of PVR to the combination of ESR and CRP, or ESR, CRP, Syn. WBC, and PMN, increased the AUC, SN, and SP for predicting PJI. Unlike alpha defensin and leukocyte esterase, which are substantially limited given their high cost and testing availability, PVR is easily calculated from routine complete blood counts with differential and yields a similar SN and SP when combined with these established serum and synovial markers. These results suggest that the combination of these markers may be a useful approach for improving the accuracy of PJI diagnosis. Further research is needed to confirm these findings and to explore the use of these markers in other populations and settings.

Conflicts of interest

N. Brown is a board or committee member for the American Academy of Orthopaedic Surgeons and a paid consultant for Corin USA, DePuy, and Johnson and Johnson Company. D. Schmitt is a paid consultant for Hip Insight; all other authors declare no potential conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2023.101195.

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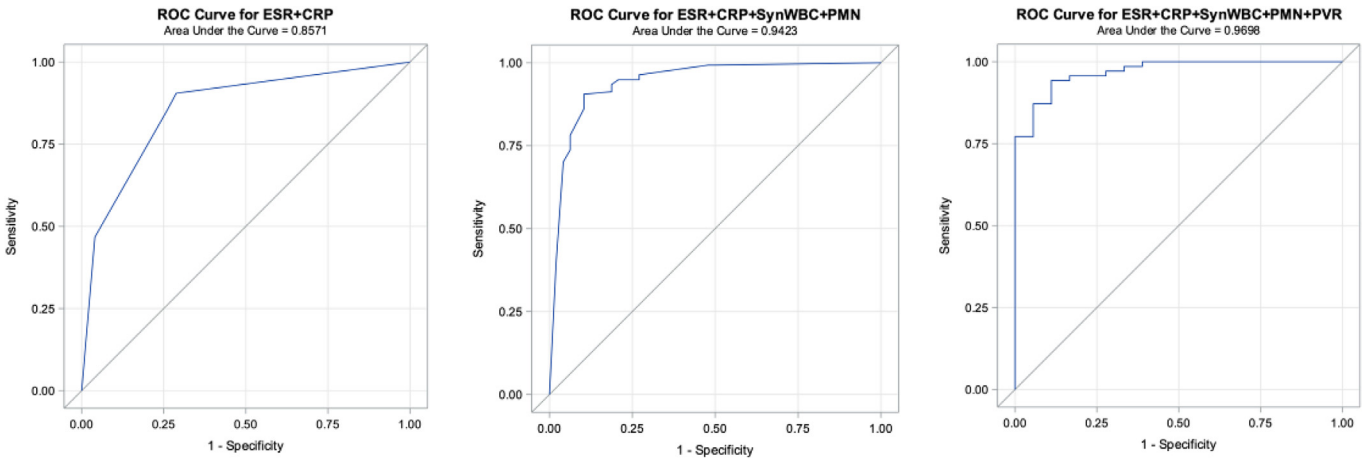
Appendix



Supplementary Figure 1. Area under the curve for established serum and synovial makers ESR, CRP, Synovial WBC, and PMN% with PVR.