

SH 40: How important are elevated ESR/CRP/WBC count/D-dimer for diagnosis of PJI? Should it they be included in the minor criteria? If so, what weighted score should it be given in the diagnostic criteria?

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Methodology: We conducted a systematic review to identify all studies evaluating the diagnostic utility of serum ESR, CRP, WBC, or D-dimer levels in shoulder arthroplasty studies. The following search string was utilized to identify studies published up until December 31, 2024:

(ESR OR "ERTHYROCYTE SEDIMENTATION RATE" OR CRP OR "C-REACTIVE PROTEIN" OR "WHITE BLOOD CELL" OR "WHITE CELL" OR "D-DIMER" OR "SERUM INFLAMMATORY") AND "SHOULDER" AND ("ARTHROPLASTY" OR "PROSTHETIC" OR "PROSTHESIS" OR "PJI") AND "SERUM"

We reviewed the titles and abstracts of all studies and excluded studies that included patients with shoulder infection without arthroplasty or patients with arthroplasty of joints other than the shoulder. The reference lists for all included studies were searched for any additional relevant articles. Only those studies that reported on the validity and performance of one of these diagnostic tests (ESR, CRP, WBC, or D-dimer) were included. Studies which only reported on means of the laboratory values but not the diagnostic testing accuracy were excluded. There were no exclusions based on the definition of shoulder PJI. Relevant data were extracted from the selected publications, including number of patients, definition of shoulder PJI, test threshold, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy.

A total of 4 studies evaluated the performance of serum ESR, 7 for serum CRP, 2 for serum WBC, and 2 for serum D-dimer in the diagnosis of shoulder PJI. It should be noted that the definition of shoulder PJI ranged from defining shoulder PJI by the presence of one positive tissue culture to individualized criteria set by the authors to the 2018 International Consensus Meeting (ICM) definition.

Response/Recommendation:

The performance of serum ESR and CRP in diagnosis of shoulder PJI varies widely in the literature, and there are limited studies evaluating serum WBC and serum D-dimer. Inclusion of these tests in the minor criteria would be based on expert opinion and would not be supported by current data in the literature.

Strength of Recommendation: Limited.

Rationale:

Shoulder prosthetic joint infection (PJI) may present along a spectrum from obvious signs of infection to minimal host response to bacteria despite positive cultures. Serum inflammatory labs including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC) count, and D-dimer levels are often obtained to help in diagnosis, but the utility of these laboratory values have been questioned.

ESR (Table I)

The 4 studies on serum ESR¹⁻⁴ used thresholds varying from 15 to 30 mm/hr. Sensitivity varied widely and ranged from 16-65%. Specificity was generally higher with a range of 58-92%. PPV and NPV ranged widely from 26-75% and 54-88%, respectively.

CRP (Table II)

The 7 studies on serum CRP¹⁻⁷ used thresholds varying from 5 to 10 mg/L. Sensitivity varied widely and ranged from 0-69%. Specificity was generally higher with a range of 44-95%. PPV and NPV ranged widely from 0-82% and 57-88%, respectively. There did appear to be a trend of increasing specificity with higher threshold values ($R^2 = 0.923$).

WBC (Table III)

There were 2 studies on serum WBC^{3,7} in the diagnosis of shoulder PJI. Despite using similar threshold values, the sensitivity and specificity were 7% and 95%, respectively, in one study, and 94% and 17%, respectively, in the other. Both report a PPV of 50%, and NPV ranged from 59-77%.

D-dimer (Table IV)

There were 2 studies on serum D-dimer^{1,5} in the diagnosis of shoulder PJI. Threshold value was 598 ng/mL in one study and 0.75 mg/L in the other. Sensitivity ranged from 61-86%, specificity from 56-74%, PPV from 35-63%, and NPV from 82-89%.

For those studies utilizing the 2018 ICM definition^{1,5,6} (which include serum ESR and CRP within the definition), the impact of using a gold standard that includes the diagnostic test itself is uncertain. The sensitivity, specificity, PPV, and NPV of serum ESR and CRP were highly variable, even when excluding the above studies. While the performance of D-dimer did appear to be stronger than other serum tests, conclusions on its utility are limited by the number of studies reporting on its performance.

These results would not support the inclusion of serum tests in the diagnostic criteria of PJI. Further study utilizing larger sample sizes, consistent definitions of shoulder PJI, and a gold standard that does not utilize the diagnostic tests itself are needed to determine if these serum studies have any value in diagnosis of shoulder PJI.

TABLE 1: ESR	Year	LOE	# of pts	PJI definition	Threshold	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
Zmistowski	2021	III	94 total 31 PJI	Definite, probable, or possible by 2018 ICM definition	28 mm/h	0.62	65%	58%	26%	88%	
Grosso	2014	III	69 total 24 PJI	Definite or probable based on criteria set by Grosso et al, JBJS 2014	15 mm/hr		42%	82%			
Villacis	2014	II	34 total 14 PJI	One positive intraoperative culture of peri-implant tissue	30 mm/hr		21%	65%	30%	54%	47%
Piper	2010	III	64 total 19 PJI	1) peri-implant purulence, 2) positive frozen, 3) sinus tract, 4) positive tissue and sonicate fluid with same organism	30 mm/hr	0.57	16%	98%	75%	73%	
Total: 4 studies						0.57 - 0.62	16-65%	58-92%	26-75%	54-88%	

TABLE 2: CRP	Year	LOE	# of pts	PJI definition	Threshold	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
Akgün	2023	II	30 total 14 PJI	Definite, probable, or possible by 2018 ICM definition	10 mg/l		69%	88%	82%	79%	80%
Akgün	2022	III	136 total 52 PJI	Definite, probable, or possible by 2018 ICM definition	7.2 mg/l	0.72	69%	74%			
Zmistowski	2021	III	94 total 31 PJI	Definite, probable, or possible by 2018 ICM definition	0.7 mg/DI	0.68	67%	60%	29%	88%	
Unter Ecker	2019	III	105 total 24 PJI	MSIS criteria (Parvizi, J Arthroplasty 2014)	5 mg/L		75%	44%	32%	84%	52%
Grosso	2014	III	69 total 24 PJI	Definite or probable based on criteria set by Grosso et al, JBJS 2014	1 mg/dL		46%	93%			
Villacis	2014	II	34 total 14 PJI	One positive intraoperative culture of peri-implant tissue	10 mg/L		0%	95%	0%	57%	56%
Piper	2010	III	64 total 19 PJI	1) peri-implant purulence, 2) positive frozen, 3) sinus tract, 4) positive tissue and sonicate fluid with same organism	10 mg/L	0.63	42%	84%	53%	78%	
Total: 7 studies						0.63 - 0.72	0-69%	44-95%	0-82%	57-88%	

TABLE III: WBC	Year	LOE	# of pts	PJI definition	Threshold	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
Unter Ecker	2019	III	105 total 24 PJI	MSIS criteria (Parvizi, J Arthroplasty 2014)	10.5/Nl	0.63	94%	17%	50%	77%	75%
Villacis	2014	II	34 total 14 PJI	One positive intraoperative culture of peri-implant tissue	11.0 X 10 ⁹		7%	95%	50%	59%	59%
Total: 2 studies						0.63	7-94%	17-95%	50%	59-77%	

TABLE IV: D-DIMER	Year	LOE	# of pts	PJI definition	Threshold	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
Akgün	2023	II	30 total 14 PJI	Definite, probable, or possible by 2018 ICM definition	0.75 mg/l	0.74	86%	56%	63%	82%	70%
Zmistowski	2021	III	94 total 31 PJI	Definite, probable, or possible by 2018 ICM definition	598 ng/mL	0.68	61%	74%	35%	89%	
Total: 2 studies						0.68 - 0.74	61-86%	56-74%	35-63%	82-89%	

References:

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