

# Improving decision making in the diagnosis of anastomotic leaks in elective colorectal cancer surgery



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## INTRODUCTION

Anastomotic leak (AL) is a potentially devastating complication of colorectal surgery. Leak rates range from 3-17%<sup>(1)</sup> and is associated with increased morbidity, 30-day mortality, utilisation of healthcare resources and prolonged hospitalisation<sup>(2-4)</sup>.

Although clinical detection of AL tend to occur between seven and 10 days but there is evidence that the physiological and biochemical changes associated with AL may occur within 36 hours<sup>(5)</sup>.

C-reactive protein (CRP) is an acute phase protein (cytokine) which is secreted 4-10 hours following inflammatory stimulation, peaks at 48 hours and has a half-life of 19 hours<sup>(6)</sup>. Previous studies have shown that the CRP level or its trajectory may predict AL<sup>(7,8)</sup>.

## OBJECTIVES

This study aims to improve the diagnosis of AL by comparing the trend and values of postoperative CRP, white cell count (WCC) and bands between patients with AL to those without an AL following elective surgery for colorectal cancer.

## METHOD

Single centre, retrospective study of prospectively collected data on patients who had an anastomosis formed following elective surgery for colorectal cancer at University Hospital Geelong from January 2005 to December 2019. Patient who had emergency colorectal surgery were excluded in this study.

Clinical information including patient demographics, method of surgery (open or laparoscopic), Duke's stage, ASA score, presence of proximal diverting stoma, biochemical and haematological markers including C-reactive protein (CRP), white cell count (WCC) and bands were collected.

Patients were analysed in two groups, those with AL and those without.

## CONCLUSION

Patients with a CRP of  $\geq 150$  on postoperative day 2 and 3 should prompt closer observation and investigation of an anastomotic leak. In these patients, surgeons should not be falsely reassured with a down trending CRP after postoperative day 3.

## REFERENCES

1. Young DE, Peterknecht E, Hajibandeh S, Torrance AW. C-reactive protein can predict anastomotic leak in colorectal surgery: a systematic review and meta-analysis. *Int J Colorectal Dis* [Internet]. 2021 Feb 8 [cited 2021 Apr 12]; Available from: <http://link.springer.com/10.1007/s00384-021-03854-5>
2. Frasson M, Flor-Lorente B, Ramos Rodríguez JL, Granero-Castro P, Hervás D, Alvarez Rico MA, et al. Risk Factors for Anastomotic Leak After Colon Resection for Cancer: Multivariate Analysis and Nomogram From a Multicentric, Prospective, National Study With 3193 Patients. *Ann Surg*. 2015 Aug;262(2):321-30.
3. Midura EF, Hanseman D, Davis BR, Atkinson SJ, Abbott DE, Shah SA, et al. Risk Factors and Consequences of Anastomotic Leak After Colectomy: A National Analysis. *Dis Colon Rectum*. 2015 Mar;58(3):333-8.
4. Turrentine FE, Denlinger CE, Simpson VB, Garwood RA, Guerlain S, Agrawal A, et al. Morbidity, Mortality, Cost, and Survival Estimates of Gastrointestinal Anastomotic Leaks. *J Am Coll Surg*. 2015 Feb;220(2):195-206.
5. Stearns AT, Liccardo F, Tan K, Sivrikov E, Aziz O, Jenkins JT, et al. Physiological changes after colorectal surgery suggest anastomotic leakage is an early event: a retrospective cohort study. *Colorectal Dis*. 2018 Dec 11;codi.14524.
6. Messias BA, Botelho RV, Saad SS, Mucchetti ER, Turke KC, Waisberg J. Serum C-reactive protein is a useful marker to exclude anastomotic leakage after colorectal surgery. *Sci Rep*. 2020 Dec;10(1):1687.
7. Smith SR, Pockney P, Holmes R, Doig F, Attia J, Holliday E, et al. Biomarkers and anastomotic leakage in colorectal surgery: C-reactive protein trajectory is the gold standard; CRP trajectory and anastomotic leak. *ANZ J Surg*. 2018 May;88(5):440-4.
8. Stephensen BD, Reid F, Shaikh S, Carroll R, Smith SR, Pockney P, et al. C-reactive protein trajectory to predict colorectal anastomotic leak: PREDICT Study: C-reactive protein trajectory to predict colorectal anastomotic leak. *Br J Surg* [Internet]. 2020 Jul 16 [cited 2020 Oct 13]; Available from: <http://doi.wiley.com/10.1002/bjs.11812>
9. Warschkow R, Beutner U, Steffen T, Müller SA, Schmiel BM, Güller U, et al. Safe and Early Discharge After Colorectal Surgery Due to C-Reactive Protein: A Diagnostic Meta-Analysis of 1832 Patients. *Ann Surg*. 2012;256(2).
10. Singh PP, Zeng IS, Srinivasa S, Lemanu DP, Connolly AB, Hill AG. Systematic review and meta-analysis of use of serum C-reactive protein levels to predict anastomotic leak after colorectal surgery. *Br J Surg*. 2014;101(4):339-46.

## RESULTS

815 patients met the inclusion criteria. The anastomotic leak rate was 3.9% (n=32). Median time to diagnosis of AL was 9 days (Range 2-18 days). The majority of patients 78.1% (25/32) were managed surgically and the remaining were managed radiologically and/or medically. There was no difference in ASA score, Dukes' staging, open or laparoscopic approach and proximal diverting stoma.

CRP levels were significantly higher in patients with AL and peaked on days 2 to 3 post-operatively and declined steadily throughout the 14 day postoperative period but with a significantly higher trajectory (p<0.05, Figure 1). WCC and neutrophils were also higher in patients with AL and but followed a different trend to CRP (Figure 2). Bands were similar between those with and without an AL.

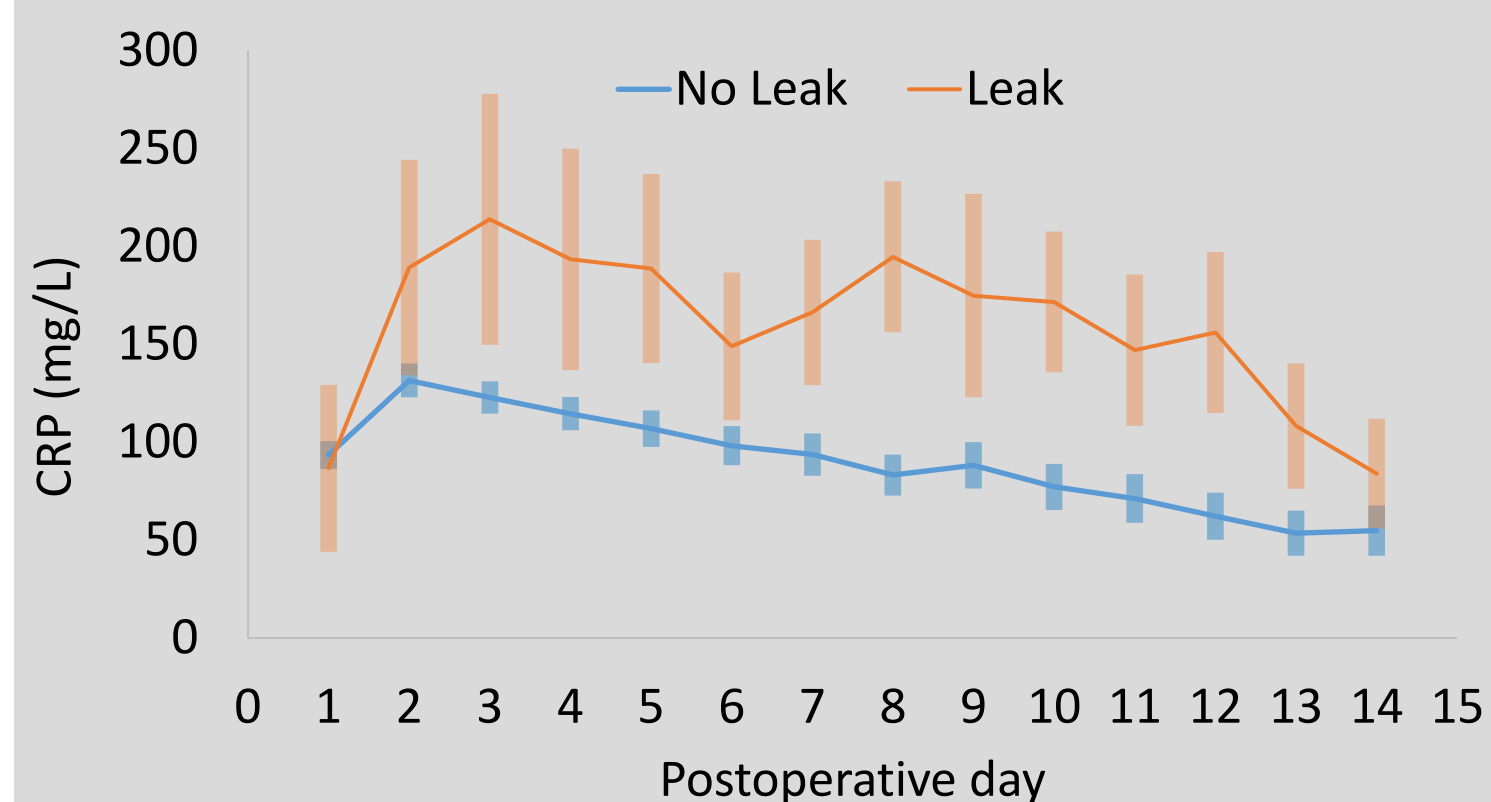


Figure 1 Mean postoperative CRP trajectory, with bars highlighting range for each data point

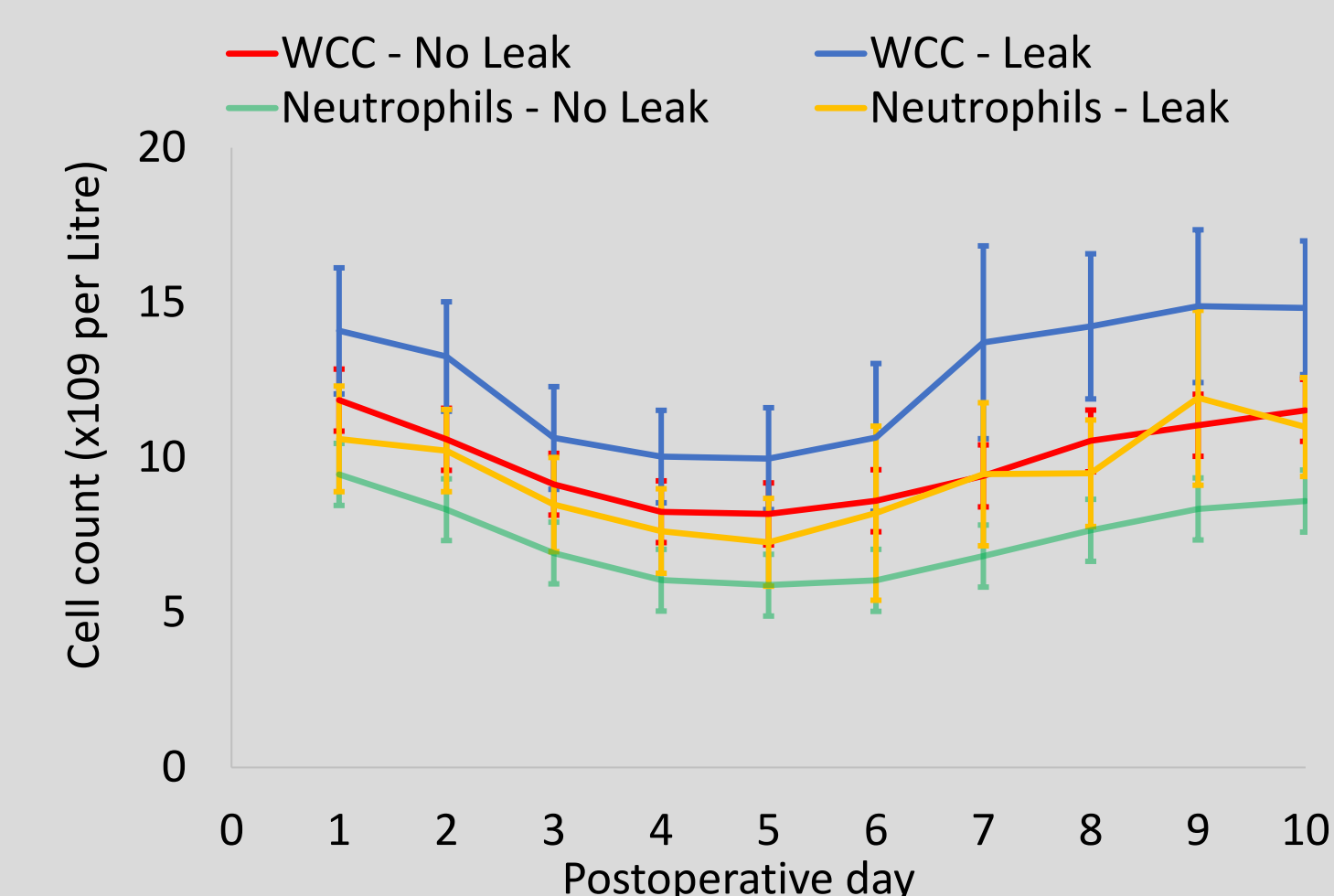


Figure 2 Mean postoperative WCC and neutrophil trajectory

## DISCUSSION

In our cohort, cut-off of 150 mg/L on day 2-3 would have included most patients with AL. The post-operative trends in CRP showed steady decline after day 2, but at higher levels in those with AL. WCC trends were also at consistently higher levels in AL but showed a lag starting from day 6 to 7. This demonstrates the superior sensitivity of CRP in detecting AL<sup>7-8</sup>. These findings echo literature, which have recommended derived CRP cut-off from 135-173 mg/L between day 3-5<sup>9-10</sup>. CRP levels should be used in conjunction with clinical findings in diagnosis of AL.

There are a few limitations in this study including small numbers and retrospective analysis, which reflects our institution's overall low AL rate.