THE LEVELS OF COLD-INDUCIBLE RNA-BINDING PROTEIN ARE MARKEDLY INCREASED IN BOTH PLASMA AND WOUND FLUID FOR A DURATION OF TWO WEEKS FOLLOWING THE RESECTION OF COLORECTAL CANCER

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Introduction

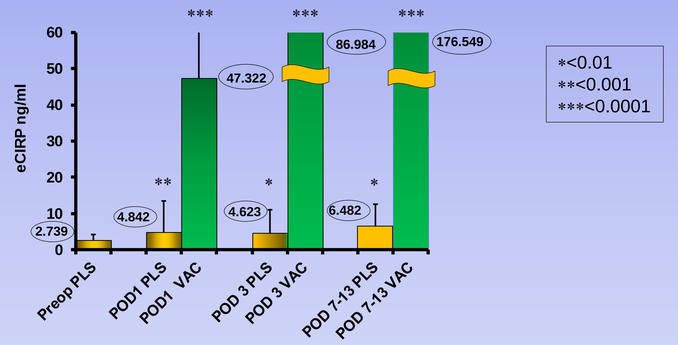
Cold-Inducible RNA-Binding Protein (CIRP) is an 18-kilodalton protein that shares similarities with a category of RNA-binding proteins that are induced by stress. Predominantly located in the nucleus, CIRP plays a crucial role in the regulation of transcription (1,2). In response to stress, CIRP translocate to the cytoplasm, where it plays a crucial role in modulating mRNA translation and degradation; a portion of the cytoplasmic CIRP is subsequently released into the extracellular space, referred to as eCIRP. (3-5). eCIRP is as a damage-associated molecular pattern (DAMP) that incites inflammatory responses and can lead to TNF-alpha, IL-6, and HMGB production (6-7). Lymphocytes, macrophages, and polymorphonuclear leukocytes (PMNs) become activated following surgical procedures and have the capacity to produce eCIRP. Elevated levels of eCIRP in the blood may influence the functionality of macrophages and foster immune tolerance, potentially facilitating tumor growth and progression (8-10).MICR is associated with significantly elevated plasma eCIRP levels for a month after colorectal cancer(CRC) resection (11). CIRP promotes the activation of AMP-activated protein kinase, and, thus, may play a role in wound healing (12). This study's objective was to determine perioperative (periop) levels of CIRP in plasma and wound fluid (WF) in patients (pts) with colorectal cancer (CRC) who had colorectal resection (CR).

Methods

The study group consisted of CRC patients who were scheduled for elective surgery enrolled in an IRB-approved tissue and data bank for whom adequate wound fluid (WF, from intra-abdominal Jackson Pratt drains) and plasma samples were available were eligible for this study. Clinical, demographic, and operative data was reviewed. Blood samples and WF were obtained simultaneously preoperatively (preop) and on postoperative (postop) day 1(POD1) and between POD 7-13; the latter were bundled into a 7-day time block and considered as a single time point. Postop samples were collected during post-discharge office appointments or follow-up visits, contingent upon the presence of the JP drain. Plasma was extracted from blood through centrifugation at 450 G, while clear wound fluid was obtained by centrifuging at 16,000 G for 10 minutes at 6° C. The centrifuged samples were stored at -80° C. eCIRP levels (ng/ml) were assessed in duplicate via ELISA; statistics were done with the Wilcoxon and Mann-Whitney tests (significance p<0.05).

Parameter	Result
Demographic & Operative Data	N =29 patients
Age, years (mean ± SD)	66.1± 12.3
Sex: Male	12 (41.0%)
Female	17 (59.0%)
Incision size :cm (mean ±SD)	
LAP Assisted procedure Hand assisted procedure Open procedures	8.3 ±3.5 11.5±3.6 23.8±7.8
Surgery time, min (mean ± SD)	459.8± 108.1
Length of stay, days (mean ± SD)	9.6± 6.3

Figure 1: Cold-Inducible RNA-Binding Protein levels in preop and post op Plasma vs. postop Wound fluids



Results

29 CRC pts (12 males, 17 females; mean age 66.10 ±12.27 years; 5 colon and 24 rectal cancers) made up the study population. 25 patients underwent minimally invasive colorectal resection (Laparoscopic; 16 pts (mean incision length: 8.3±3.5 cm), hand assisted; 8 pts (mean incision length: 11.5±3.6 cm) and 4 pts had open surgery (mean IL 23.8±7.8 cm) (Figure 2). The majority of patients underwent LAR/AR colectomy, accounting for 59%, while 24% underwent APR resection. (Figure 3)There were no major complications noted. The mean length of stay was 9.6 ± 6.3 days. Plasma levels of eCIRP were elevated on POD 1, 3, and 7-13 when compared to preop levels (P<0.001 to P <0.01). WF eCIRP levels were 10- 27 times greater than the associated plasma levels at all postop time points (P<0.0001;Figure 1)

Conclusion

Plasma eCIRP levels were elevated postop when compared to preop values. Of note, wound eCIRP levels were 10-27 times higher than plasma levels at all postop time points. This notable and profound elevation is likely related to the inflammatory responses induced by the surgery (short lived) as well as the wound healing process (of much longer duration) as well as. We hypothesize that the high wound fluid levels are the main source of the late postop plasma eCIRP elevations noted. Also, although unproven, increased plasma eCIRP levels after surgery may facilitate proliferation of residual tumor deposits.

Figure 2: Surgical procedure

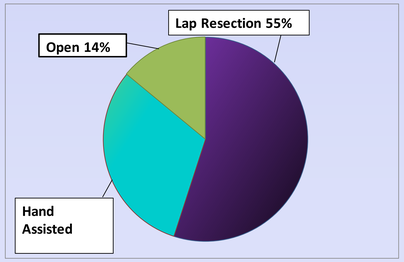
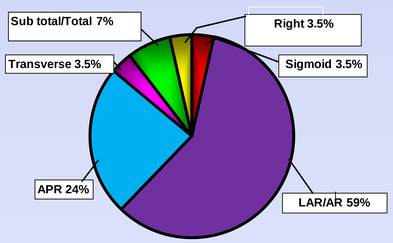


Figure 3: Types of Resection



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