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Research Article

Post-operative Carcinoembryonic Antigen (CEA) Increase as an Indicator of Recurrence After Resection in Colorectal Cancer Patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar

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ABSTRACT

Background: Carcinoembryonic Antigen (CEA) is a glycoprotein utilised as a serological marker for postoperative surveillance of colorectal cancer. Its role in predicting recurrence after curative resection remains a subject of debate.This study aimed to evaluate post-operative CEA as an indicator and predictor of recurrence after resection in colorectal cancer patients, and to determine the disease-free survival (DFS) over 24 months.

Methods: A retrospective cohort study was conducted at the Digestive Surgery Outpatient Clinic of Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, from December 2024 to February 2025. A total of 66 patients with stage II–III colorectal cancer who had undergone curative resection (R0) between 2018 and 2022 were enrolled. Post-operative CEA was measured at a minimum of four months after resection. Patients were followed for recurrence and disease-free survival over a 2-year period.

Results: Of 66 patients, 43 (65.2%) experienced recurrence. Post-operative CEA >5 ng/mL was significantly associated with recurrence (RR = 1.82; 95% CI: 1.357–2.444; p = 0.001). ROC curve analysis identified an optimal CEA fluctuation cut-off of 1.01 ng/mL as a “surveillance threshold” for predicting recurrence (AUC = 0.821; sensitivity 72.1%; specificity 95.7%). The optimal post-operative CEA cut-off was 4.11 ng/mL (AUC = 0.696; p = 0.009). Two-year DFS was significantly lower in patients with post-operative CEA >4.11 ng/mL versus those with CEA ≤4.11 ng/mL (40% vs. 63%; p = 0.001).

Conclusion: Elevated post-operative CEA was significantly associated with recurrence after resection in colorectal cancer patients. A CEA increase of 1.01 ng/mL can serve as a “surveillance threshold” to indicate possible recurrence. CEA should be combined with radiological imaging for optimal surveillance.

Keywords: Carcinoembryonic antigen; Colorectal cancer; Post-operative CEA; Recurrence; Disease-free survival

INTRODUCTION

Colorectal cancer (CRC) is a malignancy originating from the epithelial tissue of the colon and/or rectum. According to the American Cancer Society, CRC represents the third highest incidence of all cancers worldwide, with approximately 1.9 million new cases and 0.9 million deaths reported globally in 2020. The World Health Organization (WHO) projects a 77% increase in new colorectal cancer cases and an 80% rise in mortality by 2030.[1,2]

In clinical practice, managing CRC after curative resection presents a persistent challenge: patients who appear disease-free following surgery remain at substantial risk for recurrence, particularly within the first two years. Identifying these patients early, before symptoms develop, is central to improving outcomes. Post-operative surveillance using carcinoembryonic antigen (CEA) has long been part of standard follow-up protocols. Yet, its practical value has been debated, partly because a single elevated value does not always translate into detectable disease, and because the sensitivity of fixed thresholds varies widely across patient populations.

In Indonesia, CRC ranks as the fourth most common cancer, with an age-standardized incidence rate of 12.4 per 100,000 population and 35,676 new cases reported in 2022.[3] A notable characteristic in the Indonesian population is that more than 30% of cases occur in patients aged 40 years or younger, compared to only 2–8% in developed countries.[4]

Carcinoembryonic Antigen (CEA) is a 200-kDa glycoprotein found on cell surfaces that enters the bloodstream and is used as a serological marker for monitoring colorectal cancer. CEA is one of the most extensively used tumor markers for post-resection recurrence monitoring and prognosis assessment.[5,6] Normal serum CEA levels range from 2.5 to 5 ng/mL, with levels >5 ng/mL classified as elevated. Persistently elevated post-operative CEA is considered strong evidence of recurrence at the primary tumor site or the presence of distant metastasis.[7]

Locoregional recurrence occurs in 4–11.5% of patients following curative surgery for CRC and may present as peri-anastomotic, mesenteric/paracolic, retroperitoneal, or peritoneal disease. Several guidelines, including those from the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN), recommend measuring CEA every 3–6 months as part of post-operative surveillance. However, the clinical utility of CEA as a sole biomarker for detecting recurrence remains controversial, and its sensitivity and specificity have been questioned in several studies.[8,9]

Existing evidence consistently shows that a single post-operative CEA value above the conventional 5 ng/mL threshold is associated with recurrence, but this fixed cut-off has modest sensitivity and typically identifies recurrence only after substantial tumor burden has already accumulated.[10,11] What remains uncertain is whether a smaller, dynamic rise in CEA over time—occurring before the conventional threshold is crossed—can flag recurrence earlier and more reliably than a single absolute value. A threshold defined by CEA fluctuation, rather than by an isolated measurement, is therefore clinically needed to capture early recurrence signals that conventional thresholds are likely to miss, particularly in a setting where recurrence is detected relatively late.

Disease-free survival (DFS) is an important outcome measure in post-resection CRC surveillance, reflecting the duration from surgery to disease recurrence. Studies have shown that elevated post-operative CEA is associated with shorter DFS.[12,13] Furthermore, determining a specific "surveillance threshold" for CEA fluctuation may improve the early identification of patients at risk for recurrence.

To date, few studies have investigated the optimal CEA increase threshold for clinically meaningful recurrence prediction.[14] reported that a post-operative CEA increase of 1.1 ng/mL may signal early relapse. Still, this kinetic cut-off has not been formally validated using ROC-based diagnostic accuracy metrics or linked to disease-free survival outcomes. The present study extends this line of evidence by deriving an ROC-validated fluctuation threshold (1.01 ng/mL) and directly relating both fluctuation-based and absolute post-operative CEA categories to 2-year DFS, thereby providing a more complete diagnostic and prognostic characterisation than previously available kinetic-CEA studies. Therefore, this study aimed to: (1) identify the CEA increase threshold ("surveillance threshold") that predicts post-resection recurrence in colorectal cancer patients; (2) evaluate post-operative CEA as a predictor of recurrence; and (3) determine 2-year DFS rates according to post-operative CEA levels.

METHODS

Study Design and Setting

This was a retrospective cohort study with embedded diagnostic accuracy analysis conducted at the Digestive Surgery Outpatient Clinic, Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, Indonesia. Data were collected from electronic medical records of patients treated between January 2018 and December 2022. Patients were followed longitudinally from the index post-operative CEA measurement until recurrence, death, loss to follow-up, or completion of the 2-year observation period, consistent with a cohort design in which post-operative CEA category was the exposure and recurrence/DFS were the time-dependent outcomes. The study was conducted from December 2024 to February 2025.

Participants

The study population comprised all colorectal cancer patients who had undergone curative resection at the institution during the study period. **Inclusion criteria** were: (1) histopathologically confirmed primary colorectal cancer; (2) stage II or III disease based on the AJCC 2010 TNM staging system; (3) curative surgical resection with negative resection margins (R0); and (4) post-operative CEA documented in the medical record at a minimum of four months after surgery. **Exclusion criteria** included: (1) stage IV CRC; (2) multiple synchronous colorectal tumors; (3) concurrent malignancies (breast, pancreatic, pulmonary, ovarian, or prostate cancer); and (4) absent post-operative CEA records.

Sample Size

Sample size was calculated using the cross-sectional formula, based on an assumed CRC post-resection recurrence rate of 4%, a 95% confidence level ($Z\alpha = 1.96$), and an effect size of 5%, yielding a minimum of 59 samples. A total of 66 eligible patients were identified via consecutive sampling.

Variables

The independent variable was post-operative CEA level, categorised as high (>5 ng/mL) or normal (≤5 ng/mL) based on the first measurement taken at least four months post-resection. CEA fluctuation was defined as the difference between the CEA value at recurrence (or the last follow-up CEA) and the initial post-operative CEA value. The primary outcome was the occurrence of post-resection recurrence, which encompassed locoregional, systemic (hepatic, pulmonary, peritoneal), or combined recurrence, Patients were observed for a 2-year period following the index post-operative CEA measurement, and recurrence status was ascertained from documented clinical, radiological, or histopathological evidence recorded during this period. Control variables included sex, age, chronic disease history (diabetes mellitus, chronic kidney disease), tumor stage, and adjuvant chemotherapy status.

Statistical Analysis

Data were analyzed using SPSS IBM Corp.). Descriptive statistics were used to summarize sample characteristics. A chi-square test was used for bivariate analysis of the association between post-operative CEA category and recurrence, yielding relative risk (RR) estimates and 95% confidence intervals (CIs). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Receiver Operating Characteristic (ROC) curve analysis was used to determine the Area Under the Curve (AUC) and the optimal cut-off values using the Youden Index. Disease-free survival was estimated using the Kaplan–Meier method, and group comparisons were performed with the log-rank test. A p-value of <0.05 was considered statistically significant. Patients with documented post-operative CEA at a minimum of four months after resection were included; those with missing post-operative CEA records were excluded, as specified in the exclusion criteria.

Ethics

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Udayana, No: 0019/UN14.2.2.VII.14/LT/2024, and received institutional research permission from Prof. Dr. I.G.N.G. Ngoerah General Hospital. Patient confidentiality was maintained throughout.

RESULTS

Sample Characteristics

A total of 66 patients fulfilled the inclusion and exclusion criteria. Of these, 43 patients (65.2%) experienced post-resection recurrence, while 23 patients (34.8%) remained recurrence-free. This recurrence proportion is higher than that reported in many postoperative CRC cohorts and likely reflects the tertiary-referral nature of the study site, the predominance of locally advanced disease (stage IIIB/IIIC in 66.7% of patients), and the inclusion of patients with longer diagnostic delay typical of a national referral hospital; these factors are discussed further in the Limitations section. The majority were male (57.6%) and aged over 50 years (75.6%). Most patients (87.9%) had no history of chronic comorbidities. The most common tumor

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location was the rectosigmoid (77.3%), and the predominant stage at diagnosis was stage IIIC (36.4%). Histopathologically, moderate differentiation was most prevalent (42.4%). Most patients (98.5%) underwent open laparotomy, and 71.2% received adjuvant chemotherapy. Statistically, only tumor stage showed a significant difference between recurrence and non-recurrence groups (p = 0.024). Table 1 summarizes the categorical sample characteristics.

Table 1. Categorical Sample Characteristics and Association with Recurrence

Characteristic	Recurrence, n (%)	No Recurrence, n (%)	Total, n (%)	p-value
Sex				
Male	28 (42.4%)	10 (15.2%)	38 (57.6%)	0.090
Female	15 (22.7%)	13 (19.7%)	28 (42.4%)	
Age (years)				
<40	4 (6.1%)	1 (1.5%)	5 (7.6%)	0.593
40–50	6 (9.1%)	5 (7.6%)	11 (16.7%)	
>50	33 (50.0%)	17 (25.8%)	50 (75.6%)	
Tumour Stage				
Stage IIA	8 (12.1%)	9 (13.6%)	17 (25.6%)	0.024*
Stage IIB	0	3 (4.5%)	3 (4.5%)	
Stage IIIA	1 (1.5%)	1 (1.5%)	2 (3.0%)	
Stage IIIB	15 (22.7%)	5 (7.6%)	20 (30.3%)	
Stage IIIC	19 (28.8%)	5 (7.6%)	24 (36.4%)	
Tumour Location				
Right colon	4 (6.1%)	5 (7.6%)	9 (13.6%)	0.504
Left colon	3 (4.5%)	1 (1.5%)	4 (6.1%)	
Transverse colon	1 (1.5%)	1 (1.5%)	2 (3.0%)	
Rectosigmoid	35 (53.0%)	16 (24.2%)	51 (77.3%)	
Histopathology				
Well differentiated	16 (24.2%)	3 (4.5%)	19 (28.8%)	0.259
Moderately differentiated	16 (24.2%)	12 (18.2%)	28 (42.4%)	
Poorly differentiated	2 (3.0%)	1 (1.5%)	3 (4.5%)	
Mucinous	8 (12.1%)	7 (10.6%)	15 (22.7%)	
Adjuvant Chemotherapy				
Adjuvant only	28 (42.4%)	19 (28.8%)	47 (71.2%)	0.413
Neoadjuvant only	2 (3.0%)	0	2 (3.0%)	
Neo + Adjuvant	5 (7.6%)	1 (1.5%)	6 (9.1%)	
None	8 (12.1%)	3 (4.5%)	11 (16.7%)	

**Chi-square test; p <0.05 considered significant*

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CEA Data Distribution

Table 2 presents the distribution of CEA values across recurrence groups. Patients without recurrence had a mean post-operative CEA of 2.48 ng/mL and a mean CEA increase of 0.70 ng/mL. Among those with recurrence, the mean increase in CEA was 1.67 ng/mL for locoregional recurrence, 284.7 ng/mL for systemic recurrence, and 27.51 ng/mL for combined locoregional and systemic recurrence.

Table 2. Distribution of Post-operative CEA Values by Recurrence Type (ng/mL)

Group	Post-op CEA Mean (SD) ng/mL	CEA at Recurrence Mean (SD) ng/mL	CEA Increase Mean (SD) ng/mL
No Recurrence	2.48 (1.00)	–	0.70 (2.97)
Locoregional Recurrence	6.53 (4.54)	8.20 (8.09)	1.67 (5.53)
Systemic Recurrence	28.61 (97.96)	313.38 (1239)	284.7 (1227.2)
Combined (LR + Systemic)	16.50 (26.52)	44.02 (63.44)	27.51 (44.58)

Recurrence Pattern

Of 43 patients with recurrence, systemic recurrence was the most common (22 cases; 51.2%), followed by combined locoregional and systemic recurrence (16 cases; 37.2%), and isolated locoregional recurrence (5 cases; 11.6%). Among systemic recurrences, liver and lung metastases each accounted for 31.8%, while 18.2% involved other organs (brain and bone).

CEA Fluctuation as a Surveillance Threshold for Predicting Recurrence

ROC curve analysis was performed to identify the optimal CEA fluctuation threshold as a "surveillance threshold" for recurrence prediction. The optimal cut-off was a CEA increase of 1.01 ng/mL, yielding a sensitivity of 72.1% and a specificity of 95.7% (AUC = 0.821; 95% CI: 0.718–0.923; p = 0.001). This indicates that an increase in post-operative CEA of ≥1.01 ng/mL should be regarded as a signal warranting closer surveillance for impending recurrence, although the moderate sensitivity (72.1%) means that a fluctuation below this cut-off does not exclude recurrence and clinical correlation remains necessary. Table 3 and Figure 1 summarise these findings.

Table 3. Optimal CEA Fluctuation Threshold as "Surveillance Threshold" for Predicting Recurrence

Variable	AUC	Optimal Cut-off	Sensitivity	Specificity
CEA Fluctuation	0.821 (82.1%)	1.01 ng/mL	72.1%	95.7%

p = 0.001; 95% CI: 0.718–0.923

Figure 1. ROC Curve – CEA Fluctuation as a "Surveillance Threshold" for Predicting Post-resection Recurrence

Of 20 patients with post-operative CEA >5 ng/mL, 19 (95.0%) experienced recurrence, compared to 24 of 46 (52.2%) patients with CEA ≤5 ng/mL. This difference was statistically significant (χ^2 = 11.260; p = 0.001). The RR was 1.82 (95% CI: 1.357–2.444), indicating that patients with postoperative CEA >5 ng/mL had a 1.82-fold higher risk of recurrence than

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those with normal CEA levels. Table 4 presents the association between post-operative CEA and recurrence.

Table 4. Association between Post-operative CEA and Post-resection Recurrence

Post-op CEA	Recurrence, n(%)	No Recurrence, n(%)	Total, n(%)
>5 ng/mL	19 (28.8%)	1 (1.5%)	20 (30.3%)
≤5 ng/mL	24 (36.4%)	22 (33.3%)	46 (69.7%)
Total	**43 (65.2%)**	**23 (34.8%)**	**66 (100%)**

RR = 1.82 (95% CI: 1.357–2.444); χ^2 = 11.260; p = 0.001

ROC curve analysis for post-operative CEA as a predictor identified an AUC of 0.696 (69.6%; 95% CI: 0.572–0.819; p = 0.009), with an optimal cut-off of 4.11 ng/mL (sensitivity 49.0%, specificity 95.7%). The PPV and NPV were 95.0% and 47.8%, respectively. Table 5 and Figure 2 summarise these accuracy parameters. For clarity, this study uses three distinct CEA-related values that should not be conflated: the conventional 5 ng/mL value represents the established laboratory reference limit for elevated CEA (the diagnostic threshold); the 4.11 ng/mL value is the ROC-derived, statistically optimal cut-off of absolute post-operative CEA for predicting recurrence (the predictive threshold); and the 1.01 ng/mL value is the ROC-derived cut-off for the change (fluctuation) in CEA over follow-up, used as the surveillance threshold for triggering further investigation.

Table 5. Accuracy of Post-operative CEA as a Predictor of Recurrence

Variable	AUC	Cut-off	Sensitivity	Specificity	PPV	NPV	p
Post-op CEA	69.6 %	4.11 ng/mL	44.2%	95.7%	95.0 %	47.8 %	0.009

Disease-Free Survival Analysis

Kaplan–Meier survival analysis with the log-rank test revealed that 2-year DFS was significantly lower in patients with post-operative CEA >4.11 ng/mL compared to those with CEA ≤4.11 ng/mL (40% vs. 63%; p = 0.001). This demonstrates that elevated post-operative CEA is not only a predictor of recurrence but also a significant prognostic indicator of worse survival outcomes in the 2-year post-resection period. Figure 3 illustrates the Kaplan–Meier survival curves.

DISCUSSION

In this cohort, CRC predominantly affected male patients (57.6%) aged over 50 years (75.6%), a distribution broadly consistent with global epidemiological patterns in which male sex and older age are established risk factors.[4,6] The high proportion of rectosigmoid tumours (77.3%) reflects the anatomical distribution typical of CRC in Asian populations, where rectal and left-sided lesions predominate compared to Western cohorts. Among the clinical and pathological variables examined, only tumor stage reached statistical significance for predicting recurrence (p = 0.024), reinforcing the well-documented importance of TNM staging as the primary prognostic determinant in this disease. The non-

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significance of other variables, including chemotherapy status and histological differentiation, likely reflects the limited statistical power of this sample rather than true absence of effect.

Recurrence predominantly occurred in patients with stage IIIC disease (28.8%), in whom 4 to 7 lymph nodes contained tumor cells. The association between increased lymph node involvement and higher recurrence risk is well established.[8] Most recurrences were systemic (51.2%), with hepatic and pulmonary metastases each comprising 31.8% of systemic recurrence cases, consistent with previously reported patterns of CRC dissemination.[15]

CEA Fluctuation as a Surveillance Threshold

A key finding of this study is the identification of a CEA increase of 1.01 ng/mL as a "surveillance threshold" associated with recurrence (AUC = 0.821; sensitivity 72.1%; specificity 95.7%). This result is clinically significant because it provides a quantitative threshold for further investigation, even before CEA exceeds the conventional threshold of 5 ng/mL. The high specificity of 95.7% suggests that this cut-off value carries a low false-positive rate, making it a reliable trigger for additional imaging workup.

These results are corroborated by findings that a 1.1 ng/mL increase in CEA following surgery may indicate early recurrence or other pathological conditions. Similarly, Beck (2019) noted that a constant and progressive rise in CEA, particularly at a rate exceeding 12.6% per month, constitutes strong evidence of tumor recurrence. Serial CEA monitoring is currently considered the best non-invasive technique for detecting CRC recurrence.[16] Notably, CEA elevation has been reported to precede clinical manifestation of recurrence by 2.5–4 months, providing a valuable window for early intervention.[17–19]

Several biological mechanisms may plausibly explain the association between rising post-operative CEA and recurrence. First, a measurable increase in CEA may reflect residual tumor burden left after resection that was below the radiological detection threshold at the time of surgery. Second, CEA elevation may indicate micrometastatic disease that has not yet produced a clinically or radiologically apparent lesion, consistent with the observation that a rise in CEA can precede clinical recurrence by several months.[19] Third, in patients with a transient post-operative decline followed by a secondary rise, the kinetic pattern may reflect reactivation of dormant tumor cells rather than persistence of unresected disease. These mechanisms are not mutually exclusive and likely act in combination, which may partly explain why CEA fluctuation, capturing the trajectory rather than a single time point, performed better than the static cut-off in this cohort.

Post-operative CEA as a Predictor of Recurrence

Post-operative CEA >5 ng/mL was significantly associated with recurrence (RR = 1.82; p = 0.001), with 95% of patients in the elevated CEA group developing recurrence. These findings are consistent with Yang et al. (2016) and Filiz et al. (2009), who identified abnormal post-operative CEA as an independent prognostic factor for post-operative relapse, with a relative risk of 4.05 compared with patients with normal post-operative CEA levels.

The AUC of 0.696 observed in our study is comparable to the findings of Kim & Lee (2013), who reported sensitivity and specificity values of 37–46% and 90–91% in stage II and III patients, respectively. The relatively low sensitivity of post-operative CEA as a predictor of

recurrence has been a consistent finding in the literature,[10] in a meta-analysis of 12 studies, reported a pooled sensitivity of 59% for CEA (reference value: 5 mg/L) in detecting CRC recurrence, concluding that CEA alone is an insufficient biomarker for early recurrence detection.[11] similarly reported an overall test sensitivity of 38.5% using a 5 ng/mL cut-off. The modest variation in AUC across these studies likely reflects differences in case mix and follow-up: our cohort was drawn from a single tertiary referral center with a higher proportion of locally advanced (stage IIIB/IIIC) disease than the predominantly stage II-III, multicenter populations reported by previous research[20,21] and in the meta-analysis[22] also our 2-year follow-up window is shorter than the 3-5 year horizons used in several comparator studies, which may inflate the apparent discriminatory performance of an early post-operative CEA value by enriching for early, more biologically aggressive recurrences. These findings reinforce the recommendation by major guidelines (ASCO, NCCN) to combine CEA monitoring with radiological imaging for optimal surveillance.

Our study demonstrated that patients with post-operative CEA >4.11 ng/mL had a 2-year DFS of only 40%, compared to 63% in those with CEA ≤4.11 ng/mL (p = 0.001). These results are consistent with those of,[23] who found that elevated post-operative CEA was associated with shorter recurrence-free survival in a cohort of 761 colon cancer patients, and with,[24] who reported a 3-year relapse-free survival of 60% versus 87.5% in patients with high versus normal post-operative CEA (p <0.001).[25] also demonstrated that early recurrence (within 1 year of surgery) was associated with poor overall survival, underscoring the prognostic importance of post-operative surveillance.

The prognostic significance of post-operative CEA for DFS supports its integration into routine surveillance protocols. However, as highlighted by the utility of CEA is maximized when combined with intensive imaging modalities; combining CEA measurement with CT scanning has been shown to detect asymptomatic recurrences in up to 90% of cases.[25,26] Accordingly, current RCT evidence suggests that CEA measurement every 3–6 months combined with CT scanning at 12–18 months can triple the proportion of patients eligible for curative retreatment.

In practical terms, these findings suggest a tiered surveillance pathway: a CEA fluctuation reaching the 1.01 ng/mL surveillance threshold, particularly when accompanied by an absolute value approaching 4.11 ng/mL, could reasonably trigger earlier cross-sectional imaging (CT chest/abdomen/pelvis) rather than waiting for CEA to exceed the conventional 5 ng/mL diagnostic threshold or for symptoms to develop. Because CEA testing is inexpensive relative to CT or MRI, using fluctuation as a pre-screening trigger may help concentrate imaging resources on patients at highest risk, which could be particularly relevant in resource-limited settings; however, the cost-effectiveness of this strategy, including the cost of false-positive imaging triggered by the 72.1% sensitivity/95.7% specificity profile, has not been formally evaluated in this study and would need to be assessed prospectively before the threshold is adopted into routine surveillance pathways.[27–30]

Public health perspective

Because CEA testing is inexpensive and widely available, a validated surveillance threshold could, in principle, support more efficient allocation of imaging resources in CRC follow-up, which may be relevant given the substantial and rising burden of CRC in Indonesia.[31]

However, this study is a single-center clinical prognostic analysis rather than a population-level or health-economic study, and these broader public health implications are extrapolations that have not been directly tested here; they should therefore be regarded as hypothesis-generating pending dedicated health-systems and cost-effectiveness research.

This study has several limitations. The retrospective design and reliance on medical record data introduce potential selection bias and information bias. The single-center nature of the study may limit generalisability. Additionally, the 2-year follow-up period may not fully capture late recurrences, and the relatively small sample size limits the statistical power of subgroup analyses. Associations between post-operative CEA and recurrence were assessed using bivariate analysis only, without adjustment for potential confounders such as tumor stage, histology, chemotherapy, age, and tumor location; the reported associations should therefore be interpreted as unadjusted. The proposed surveillance threshold has not undergone external validation in an independent cohort, and no serial (longitudinal) kinetic modeling of CEA trajectories was performed, which may have provided a more sensitive characterization of recurrence risk than the single fluctuation value used here. Future prospective multicentre studies are warranted to validate the identified CEA surveillance threshold and its integration with imaging surveillance protocols. Such studies should incorporate multivariable adjustment, external validation, and longitudinal CEA kinetic modeling.

CONCLUSION

Post-operative CEA demonstrated moderate discriminatory ability for recurrence prediction in patients with stage II–III colorectal cancer and may complement imaging-based surveillance after curative resection. A CEA increase of 1.01 ng/mL can be considered a “surveillance threshold” warranting further clinical investigation. The optimal post-operative CEA cut-off of 4.11 ng/mL yields the best predictive accuracy (AUC = 0.696). Patients with post-operative CEA >4.11 ng/mL have a significantly lower 2-year DFS (40% vs. 63%; p = 0.001). CEA monitoring should not be used as a standalone biomarker but should be combined with radiological imaging to optimize early recurrence detection and improve patient outcomes. These findings should be regarded as hypothesis-generating rather than practice-changing; prospective multicentre validation, longitudinal surveillance studies, and external ROC validation are needed before the 1.01 ng/mL surveillance threshold is recommended for routine clinical implementation.

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Declarations

Authors' contributions

CGBNP contributed to the study conception and design, data collection, data analysis and interpretation, and drafting of the manuscript. I.B.M.S. contributed to the research design,

supervision of data analysis, critical revision of the manuscript for important intellectual content, and final approval of the version to be published. K.S. contributed to data interpretation, methodological input, and critical review of the manuscript. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Conflict of interest

The authors declare no conflict of interest

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