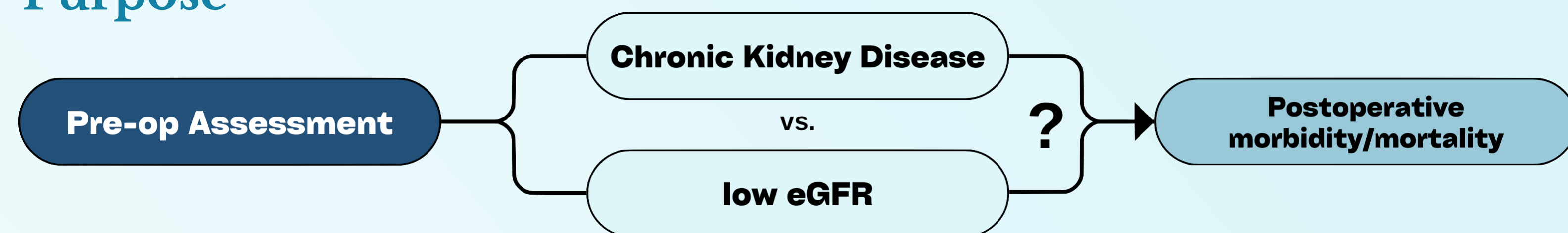


Surgical Crossroads: How Chronic Kidney Disease Alters Colorectal Cancer Surgery Outcomes

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Purpose



Introduction

The rising prevalence of colorectal cancer (CRC) and chronic kidney disease (CKD) presents a significant healthcare challenge in an aging population. Australia has witnessed a dramatic increase in colorectal cancer cases, from 6,988 cases in 1982 to over 15,000 new cases in 2023. Simultaneously, the number of Australians affected by moderate to severe kidney dysfunction has doubled since 2000, now exceeding 600,000 individuals.

The coexistence of these conditions creates unique challenges in perioperative management. CKD's pathophysiological mechanisms, including enhanced oxidative stress, proinflammatory cytokine production, and endothelial damage, may significantly impact surgical outcomes. Despite the clinical importance, current literature shows conflicting evidence regarding the relationship between CKD and postoperative outcomes in colorectal surgery.

Methods

Study Design:

- Retrospective analysis of 2,286 patients using a high-quality prospective clinician-led database
- Multiple centers: Cabrini Malvern, Alfred Hospital, Monash Hospitals, Peninsula Health
- Period: January 2010 - December 2023

Inclusion Criteria:

- Age >18 years
- Underwent CRC resection
- Non-metastatic disease
- Curative intent
- Complete renal function data

Statistical Analysis:

- Multivariable logistic regression
- Cox proportional hazards regression
- Kaplan-Meier survival analysis
- Inverse probability weighting for missing data

Results – Short Term Outcomes

Our analysis revealed that CKD, present in 135 patients (5.9%), served as an independent predictor of adverse postoperative outcomes. After adjusting for confounding factors, CKD demonstrated significant associations with increased postoperative complications (ARR: 1.33, p=0.018), 30-day mortality (AHR: 8.83, p=0.003), and prolonged ileus (AHR: 1.46, p=0.017).

The impact of preoperative eGFR <60 mL/min/1.73m², showed a distinct pattern. While initially associated with medical complications and mortality in univariate analysis, these associations lost significance after multivariate adjustment. However, reduced eGFR maintained significant associations with decreased risk of chest infection (ARR: 0.56, p=0.001) and prolonged ileus (ARR: 0.75, p=0.008).

OUTCOME	CKD NO (n=2151)	CKD YES (n=135)	P-value	Adjusted HR/RR (95% CI)
Surgical Complications	17.2%	28.1%	0.001	1.38 (0.81 - 2.35)
Medical Complications	10.3%	22.2%	<0.001	1.07 (0.60 - 1.91)
Any complications	24.3%	43.0%	<0.001	1.33 (1.05 - 1.68)
30-day Mortality	0.5%	3.0%	<0.001	8.83 (2.07 - 37.72)
5-year survival	83.3%	58.9%	-	-
Overall Mortality	11.4%	24.4%	<0.001	1.60 (1.43 - 1.80)
Prolonged Ileus	7.1%	14.1%	0.003	1.46 (1.07 - 2.00)
Cardiac complications	2.8%	7.4%	0.003	1.21 (0.47 - 3.16)
Return to theatre	6.0%	8.9%	0.184	0.90 (0.54 - 1.51)

Table 1: CKD Status and Its Association with Postoperative Morbidity and Mortality

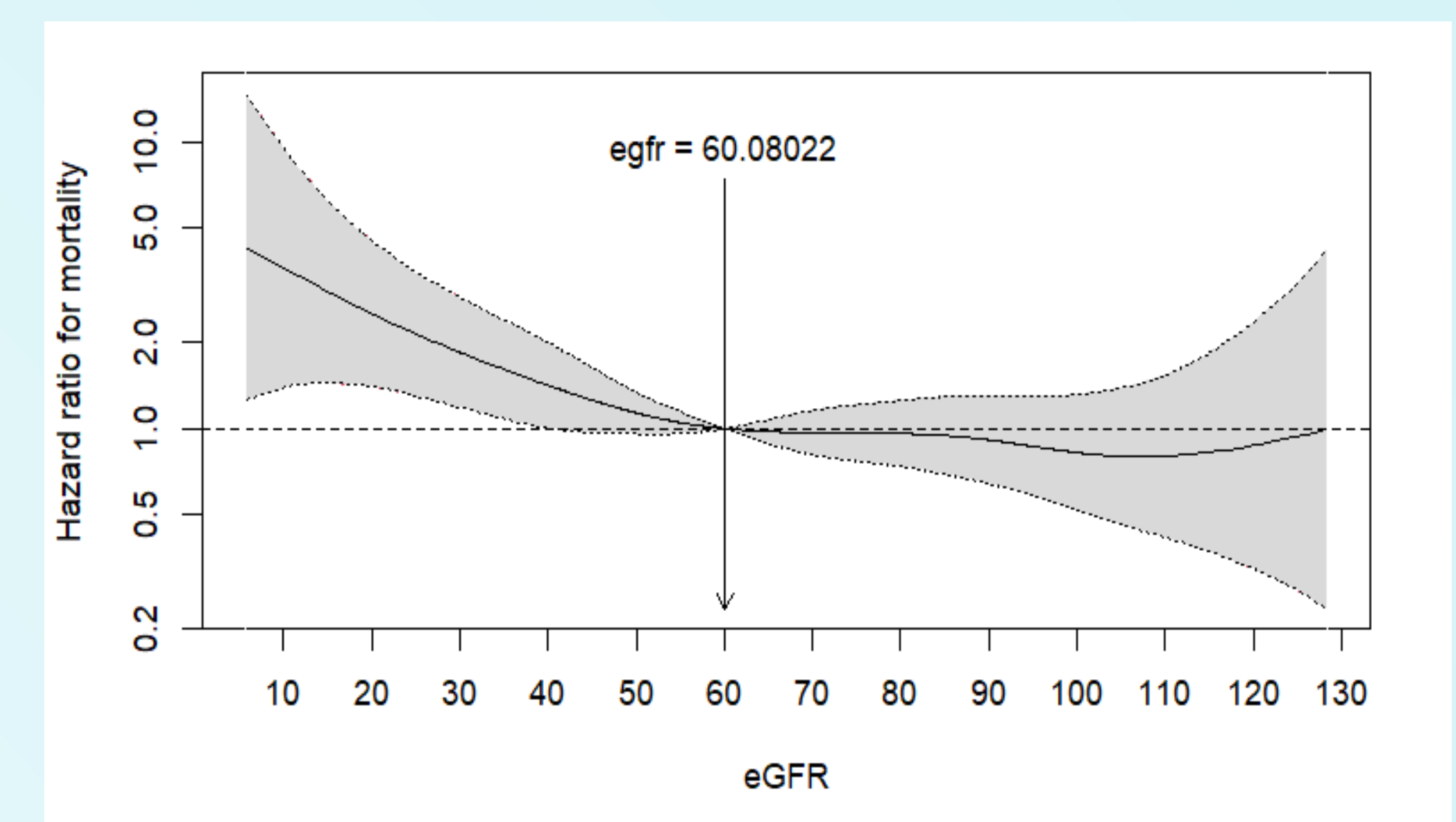


Figure 1: Overall hazard of mortality vs continuous eGFR from the multivariable analysis

Results – Long Term Outcomes

Long-term survival analysis demonstrated substantial disparities between CKD and non-CKD patients. Five-year overall survival rates were markedly lower in CKD patients at 58.9% compared to 83.3% in non-CKD patients. Similarly, five-year relapse-free survival rates showed significant differences: 57.4% for CKD patients versus 82.7% for non-CKD patients.

Multivariate analysis confirmed CKD as an independent predictor of both overall mortality (AHR: 1.49, p<0.001) and relapse-free mortality (AHR: 1.51, p<0.001). These findings remained robust after adjusting for numerous potential confounding factors, including age, comorbidities, and cancer stage.

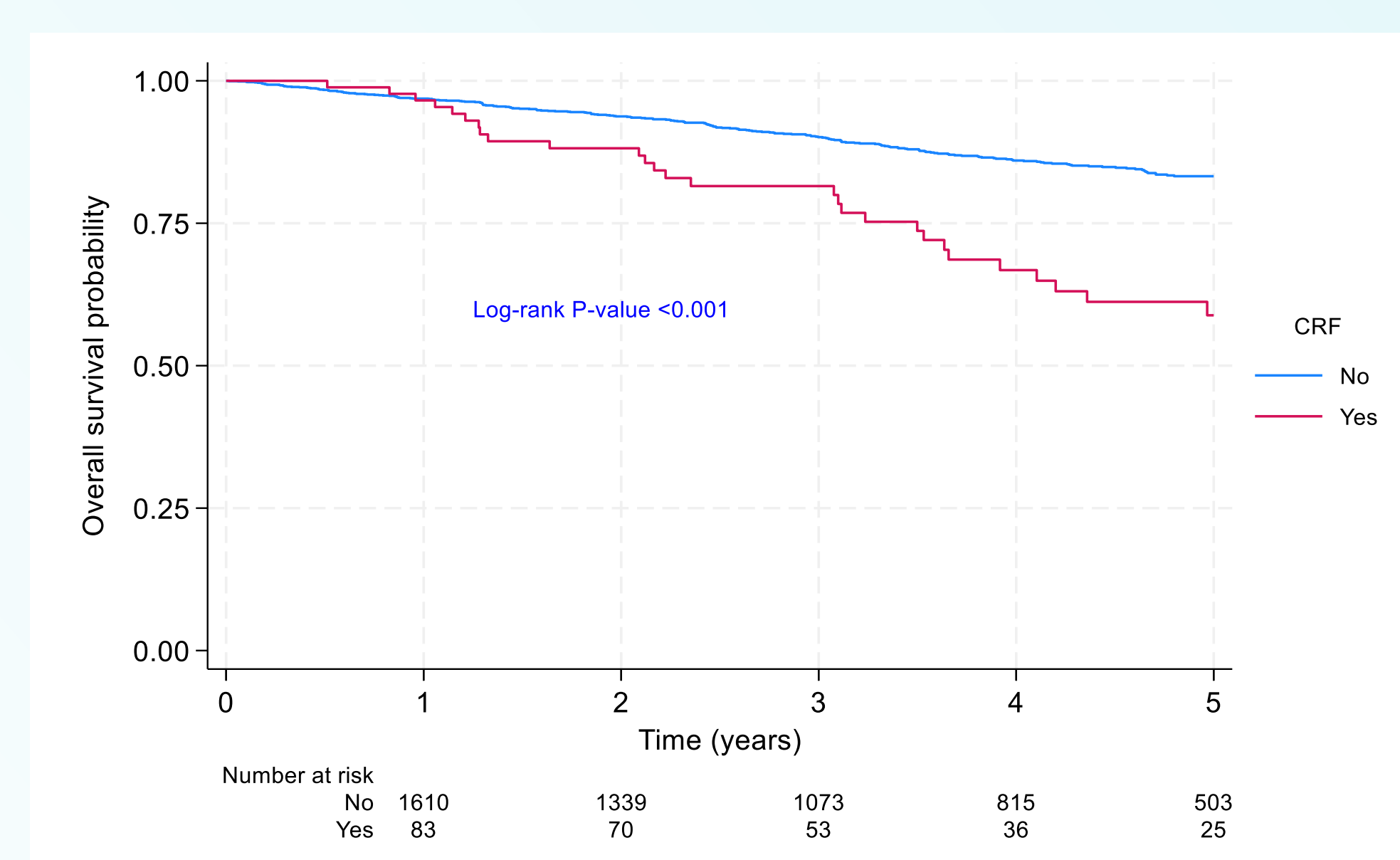


Figure 2: Overall survival stratified by CKD status

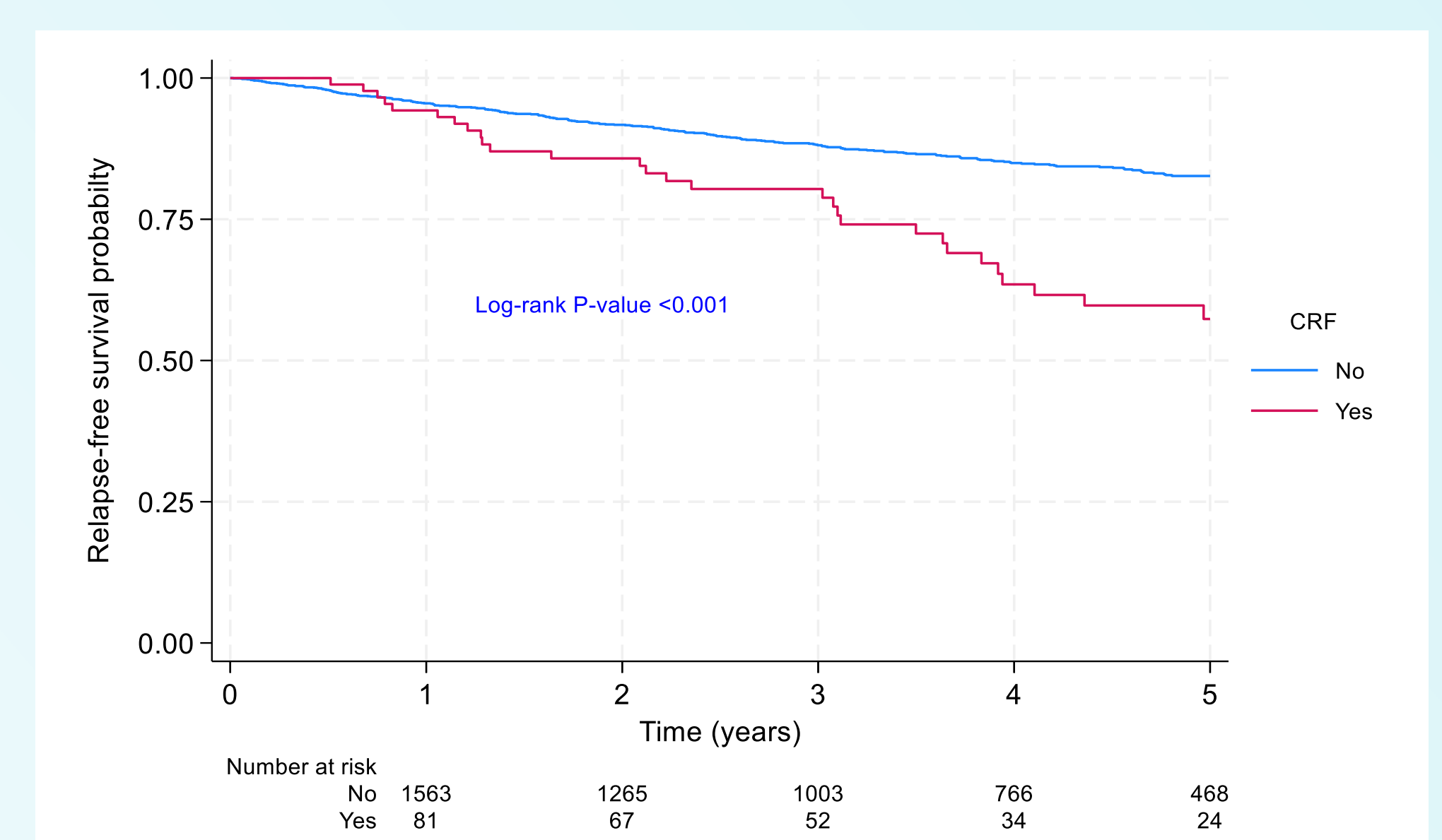


Figure 3: Relapse-free survival stratified by CKD status

Key Findings

CKD is a superior predictor of postoperative complications after CRC surgery compared to single eGFR measurement

Significant impact on:

- Short-term complications
- 30-day mortality (8.83x increased risk)
- 5-year survival (24.4% absolute reduction)
- Overall and relapse-free survival

Limitations of preoperative measurement of eGFR :

- Low index of individuality (0.3)
- Influenced by sarcopenia in CRC patients
- Less significant association with postoperative outcomes

The marked difference in survival rates between CKD and non-CKD patients suggests the need for specialized perioperative protocols for this high-risk population. The complex interplay between CKD, surgical stress, and CRC outcomes warrants careful consideration in perioperative planning and management

Clinical Implications

These results highlight the critical importance of comprehensive preoperative renal function assessment in colorectal cancer surgery patients. The strong predictive value of CKD for both short-term complications and long-term survival suggests the need for risk stratification and tailored perioperative management strategies for this vulnerable population.

Implementation of specialized care protocols, including careful monitoring of fluid status, medication adjustments, and enhanced postoperative surveillance, may help mitigate the increased risks associated with CKD in this surgical population.

Future Directions and Limitations

Future Research Needs:

- Prospective validation studies
- eGFR range classification analysis
- Investigation of eGFR <45mL/min cutoff
- Optimization of perioperative protocols

While our study benefits from a large, clinically validated database, some limitations warrant consideration. The retrospective design may introduce selection bias, and the relatively low prevalence of CKD (6%) in our cohort may affect generalizability. Additionally, some complications were determined by clinical rather than laboratory criteria.