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Resting Heart Rate is a Prognostic Factor for Mortality in Patients with Colorectal Cancer

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ABSTRACT

INTRODUCTION: Colorectal cancer is a leading cause of death in the world and US. Although the colorectal surgery reduces overall mortality rate, there are individual variations (exhibiting 50-90% of 5-year survival rate after the surgery). In this regard, an accurate prediction (using preoperative characteristics) of mortality after the sugery in colorectal cancer patients has been highlighted. One such modifiable prognostic indicator of mortality is resting heart rate (RHR). To date, elevated RHR was reported to be highly associated with increased mortality rate in the general population and patients with various cancers such as lung and breast cancer. However, there is lack of evidence to support whether RHR at the day of surgery could indicate mortality in patients with colorectal cancer over time.

PURPOSE: We aimed to see if RHR is a significant predictor of all-cause and cancer-specific mortality in patients with colorectal cancer who underwent colon or rectal cancer surgery.

METHODS: Baseline data from the Severance Hospital Colorectal Cancer Registry (from December 2010 through December 2015) was utilized for the present retrospective study with ongoing follow-up screening (~10 years), including a total of 3,547 colorectal cancer patients with stage I-III who underwent colon or rectal cancer surgery. The Registry Database includes physical examination (weight, height, BMI, blood pressure), disease history, date and types of surgery, location of the primary tumor, TNM (tumor, node, metastasis) stage, histology, the number of lymph node, ASA score, the regimen of adjuvant therapy, alcohol and smoking history, and follow-up outcomes related to colorectal cancer. All of the aforementioned varilables were used as covariates for the analysis. RHR (beats per minute; bpm) data were collected on the day of surgery after >5 min of resting in a supine position. The primary outcomes were (1) all-cause mortality calculated from the date of colorectal cancer surgery to the date of the death from any cause, and (2) colorectal cancer-specific mortality collected from the medical chart review. Analysis of variance and χ^2 test were used to compare the

patients' baseline characteristics. Multivariable Cox-proportional hazards models were conducted to estimate hazard ratios (HRs) of RHR with 95% confidence interval (CI) for all-cause mortality and colorectal cancer-specific mortality. All statistical analyses were conducted by SAS 9.4 (SAS, NC, USA) with a level of significance set at p value <0.05.

RESULTS: A total of 3,547 colorectal cancer patients was divided into 5 groups based on their RHR: Quintile 1 [Q1] (≤66 bpm); Q2 (67-73 bpm); Q3 (74-80 bpm); Q4 (81-88 bpm); and Q5 (≥89 bpm). At baseline, Q5 had more disease histories, number of positive lymph node, poor histology, and higher TNM stage among the groups. Over the 10-years follow-up period, 320 death cases from all-cause and 202 death cases from colorectal cancer-specific were reported. There was a significant and prospective relationship between RHR and all-cause mortality in unadjusted and adjusted models: (unadjusted HR Q5 vs. Q1: 4.46, 95 % CI: 2.26-6.96) and (adjusted HR Q5 vs. Q1: 4.26, 95 % CI: 2.68-6.78). Similarly, RHR is significantly predictive of colorectal cancer-specific mortality: (unadjusted HR Q5 vs. Q1: 4.46, 95 % CI: 2.26-6.96) and (adjusted HR Q5 vs. Q1: 4.26, 95 % CI: 2.68-6.78). It is notable that HRs (95 % CI) for all-cause mortality and colorectal cancer-specific mortality with RHR per 10 bpm increase was 1.46 (1.34 -1.59) and 1.49 (1.34 - 1.65), respectively.

CONCLUSION: Increased RHR was associated with all-cause and colorectal cancer-specific mortality in patients with colorectal cancer who underwent the surgery. It could be postulated that elevated RHR reflects an increased sympathetic nerve system, which might affect the beta-adrenergic signaling that contribute to cancer progression (i.e., worsen mortality even after the surgery). In line with this theory, our data suggest that baseline RHR of the colorectal cancer patients who will have their surgery can be a clinically relevant prognostic indicator of future mortality. Further research should be warranted to identify efficient strategies to modify RHR prior to the surgery to improve overall survival in colorectal cancer patients.

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