中文題目：癌症病人 QT 延長與心血管死亡的相關性

英文題目：The QT interval and cardiovascular mortality in cancer patients

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Background: The QTc intervals have been used to guide drug therapy based on its risky link to ventricular arrhythmias in cancer patients. Surprisingly, until now, the real impact of a QT interval on cardiovascular (CV) mortality in cancer patients has not been investigated in a large patient cohort. We aim to analyze whether a QT interval would be a suitable predictor for CV mortality in a large hospital-based patient cohort and decide the best QTc formula for clinical application in cancer patients.

Methods: In cancer patients, we collected the first performed electrocardiograms (ECGs) after a cancer diagnosis from 2008 to 2020 at Taipei Veterans General Hospital, Taiwan. In non-cancer patients, the first available ECGs were collected in the same period to serve as a comparison control. Cancer and non-cancer patients were matched for age and sex using propensity score analysis. The Bazett (QTcB), Fridericia (QTcFri), and Framingham (QTcFra) QTc formulas were used to predict the 90-day and 1-year CV death. An adapted Cox proportional hazards regression model was used to estimate the independent impact of QTc >500ms on CV death.

Results: A total of propensity score-matched age and sex cancer (n=59,568) and non-cancer (n=59,568) patients were enrolled. First, by the model of univariate analysis, the corrected QT intervals were significantly associated with CV death both in cancer and non-cancer patients. The area under curves (AUC) for the prediction of a 90-day and 1-year CV death were better by QTcB (: 0.70 and 0.68) than

QTcFri and QTcFra (Figure 1). However, the predictive power for CV death was less in cancer than in non-cancer patients (AUC: 0.76 [90-day] and 0.73 [1-year]). Cancer patients with QTcB ≥500ms had a 5.98 and 4.61-fold risk of 90-day and 1-year CV death, respectively. However, after multivariate analysis with comorbidities, QTcB could not independently predict both 90-day and 1-year CV death (Figure 2). Rather than a long QTc interval per se, complex comorbidities in cancer patients contributed to a higher CV death in cancer patients with a long QTc interval.

Conclusions: The QTc interval might be considered a biomarker reflecting complex comorbidities, but not an independent predictor for CV death in cancer patients. The QTcB is a better formula for predicting CV mortality in cancer patients.

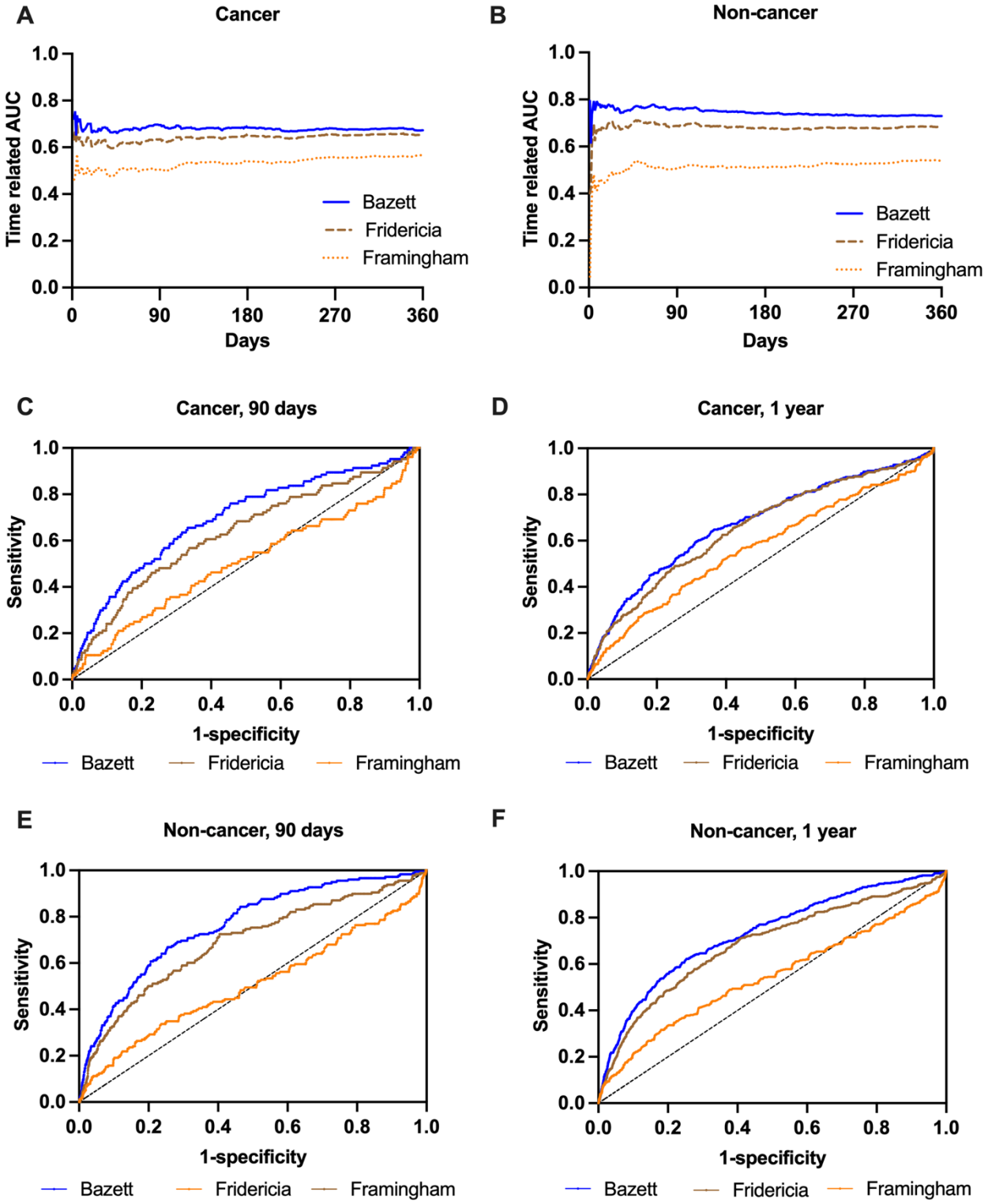

Figure 1. Time-dependent AUC for CV death in different QTc formulas. A and B. The QTcB had better performance in prediction of CV mortality in both cancer and non-cancer patients. **C and D.** In cancer patients, the AUCs for the prediction were better with QTcB than QTcFri and QTcFra at 90-day (QTcB vs. QTcFri, p = <0.001; QTcB vs. QTcFra, p = <0.001) and 1-year CV death (QTcB vs. QTcFri, p = <0.0233; QTcB vs. QTcFra, p = <0.001). **E and F.** The AUCs for predicting CV death

were also better with QTcB than QTcFri or QTcFra in non-cancer patients at 90-day (QTcB vs. QTcFri, p = <0.001; QTcB vs. QTcFra, p = <0.001) and 1-year (QTcB vs. QTcFri, p = <0.001; QTcB vs. QTcFra, p = <0.001). Abbreviation: AUC, area under the curve; CV, cardiovascular; QTcB, QTc Bazett formula (QTcB= QT/ $RR^{1/2}$); QTcFri, QTc Fridericia formula QTcFri= QT/$RR^{1/3}$; QTcFra, QTc Framingham formula (QTcFra= QT+ 0.154[1-RR]) patients.

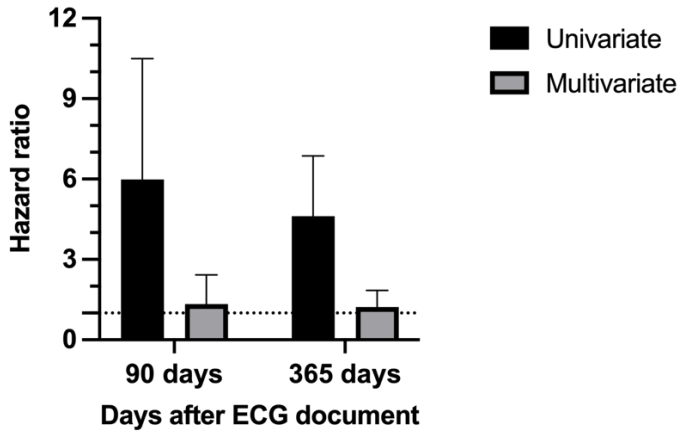

Figure 2. The hazard ratios of CV death at the QTcB ≥500ms.

Cancer patients with QTcB ≥500ms had a 5.98 and 4.61-fold risk of 90-day and 1-year CV death, respectively, in univariate analysis. However, after adjusting multiple comorbidities (HTN, DM, HF, MI), and risk factors (heart rate, gender, age) in multivariate analysis, QTcB could not independently predict both 90-day and 1-year CV death. Abbreviation: CV, cardiovascular; DM, diabetes mellitus; HF, heart failure; HTN, hypertension; MI, myocardial infarction; QTcB, QTc Bazett formula (QTcB= QT/ $RR^{1/2}$).