Abstract— In this paper we introduce Gamma probability distribution model is used to obtain the survival rates of the patients [2,6,8]. The Gamma distribution is extensively used in engineering, reliability and applied statistics. This distribution is a reasonable model to describe the progression of colorectal cancer and finding survivor rate estimates for the medical data. Mesothelin is a cell surface protein and over expressed in many cancers. However, the potential value of mesothelin as plasma biomarker in colorectal cancer has not been explored. The purpose of this study was to identify whether plasma mesothelin is a suitable diagnostic and prognostic biomarker for colorectal cancer. The application part is fitted with the Mathematical model and conclusion is compared with the medical report. This will be helpful for the medical professional.

Key words: Mesothelin, Colorectal Cancer, Biomarker, Gamma Distribution

I. INTRODUCTION

Colorectal cancer is the third most common malignant tumor by incidence around the world [7]. About 134,490 new cases will be diagnosed with colorectal cancer in 2016, estimated by the American Cancer Society [17]. However, nearly 25% patients with colorectal cancer were diagnosed advancing stage at the first time, and the 5-year survival rate of colorectal cancer was estimated to be 62%-64% [12, 14]. Due to the limitation of the screening tests in the early diagnosis of colorectal cancer, it is necessary to identify new potential biomarkers, especially in plasma or serum, for the diagnosis of colorectal cancer and prediction of therapy. Mesothelin, a 40-kDa cell glycosylphosphatidyl inositol (GPI)-linked protein, has been found in mesothelial cells lining the peritoneum, pleura and pericardium usually [4, 5]. The over expressed mesothelin has been detected in mesothelioma and pancreatic cancer [16, 13]. Mesothelin over expression has also be found in many other cancers in serum and other body fluids, including ovarian malignancies, gastric cancer and lung adenocarcinomas [9,10,15]. The biological function of mesothelin with colorectal cancer in vitro [14]. Moreover, the significantly over expressed mesothelin was identified in colon cancer serum [3]. In this study, we investigated the level of mesothelin in plasma in a two-stage case-control study and evaluated the diagnosis and prognosis value of colorectal cancer patients with high mesothelin level. Moreover, we estimated the difference of mesothelin level between preoperative plasma and postoperative plasma samples.

II. APPLICATION:

A total of 147 patients with colorectal cancer and 121 healthy controls were recruited in this study. In the first stage, 40 primary colorectal cancer cases were pathologically confirmed in the Third Affiliated Hospital. Forty cancer-free controls were recruited from those seeking medical care in local hospitals with frequency-matched to cases on age (± 5 years) and gender. In the second stage, 107 colorectal cancer cases and 81 controls were recruited from the First Affiliated Hospital. A total of 54 patients’ were followed-up through telephone calls at regular intervals for up to 5 years and the median survival time (MST) was 41.3 months. There were 147 colorectal cancer cases and 121 cancer-free controls in this two-stage case-control study. The average age of cases and controls was 60.7 and 59.6 respectively, and no significant differences between patients and controls were identified in age (P = 0.858) and sex (P = 0.050). In addition, we found no notable differences in drinking and smoking status between two groups (P > 0.05). However, significantly increased frequency of family history of cancers was found in colorectal cancer group (P < 0.001).

Figure 2.1: Preoperative plasma mesothelin levels in healthy controls and colorectal cancer patients under different Duke’s stages.

Box plots represent plasma mesothelin levels in healthy controls (n = 121) and colorectal cancer cases (n = 147) and patients under different Duke’s stages (A + B; n = 74, C+D; n = 73). Boxes indicate the interquartile range, and median values are shown by the horizontal lines across boxes. Statistically significant differences were determined using two-sided Wilcoxon test. **P < 0.001.

Fig. 2.2: Kaplan-Meier curves of overall survival for plasma mesothelin levels in colorectal cancer patients:
The cutoff value of plasma mesothelin was derived by Youden index (36.50ng/ml). High group represents patients with plasma mesothelin higher than 36.50 ng/ml (n = 27) and Low group represents patients with plasma mesothelin lower than 36.50 ng/ml (n = 27).

III. MATHEMATICAL MODEL

The gamma distribution has also received considerable attention in the area of weather analysis. The two-parameter gamma distribution of a random variable T has a pdf of the form

\[ f(t; \lambda, \alpha) = \frac{\lambda^{\alpha} t^{\alpha-1} e^{-\lambda t}}{\Gamma(\alpha)}, t \geq 0 \]

where \( \lambda > 0 \), and \( \alpha > 0 \) are the scale and shape parameters of the gamma density function respectively, and

\[ \Gamma(\alpha) = \int_0^\infty y^{\alpha-1} e^{-y} dy \]

From the above gamma density function, if we take \( \alpha = 1 \) the gamma density function reduces to exponential death density function. If \( \alpha > 1 (<1) \), then the failure rate or hazard rate of the gamma density function increases (decreases) as a function of time.

IV. MATHEMATICAL RESULTS:

![Graph showing probability density function]

Fig. 4.1: Probability density function

V. DISCUSSION

Patients with lower mesothelin in plasma had longer survival time, compared with patients whose mesothelin levels were higher than 36.50 ng/ml (log-rank \( P < 0.001 \)). Furthermore, cox regression analysis revealed that there were statistically significant associations between elder individuals, drinkers and lower survival time (adjusted HR = 2.83, 95% CI = 1.33-6.00, \( P = 0.007 \); adjusted HR = 3.72, 95% CI = 1.26-11.0, \( P = 0.018 \)). However, when stratified by sex, smoking status, tumor size, grade and we observed no significant difference in survival time in each following subgroup compared with each above subgroup (log-rank \( P > 0.05 \)). We also found that patients with higher levels of plasma mesothelin had a prominent poor prognosis than those with lower mesothelin levels (adjusted HR = 4.43, 95% CI = 1.93-10.15, \( P < 0.001 \)). In addition, unadjusted survival curves demonstrated a significant difference in 5-year survival between higher and lower level of mesothelin in colorectal cancer patients. As shown in Figure 2.2, patients with high level of mesothelin had a worse survival than patients with lower level of mesothelin (\( P = 0.001 \)).

Previous studies have demonstrated that mesothelin can regulate growth and apoptosis in cancers [18]. Some studies suggested that mesothelin was associated with lymphatic invasion of colorectal cancer and over-expressed mesothelin in serum has potential ability to detect and screen colon cancer [12,3]. Serum or blood mesothelin was suggested to be potential biomarker for early diagnosis or survival time in many cancers [11,1]. However, the utility of mesothelin as biomarker in colorectal cancer was plasma samples should be included to identify the association of mesothelin with the effect of tumor resection.

VI. CONCLUSION

We have identified the plasma mesothelin as a potential biomarker with diagnosis and prognosis values in colorectal cancer, which was significantly increased in colorectal cancer cases, compared with controls. The medical curve and Mathematical curve for disease control is higher than the probability density functions which are monotonic functions. We conclude that our mathematical result is well fitted in the Gamma distribution.

REFERENCES